(FILE 'HOME' ENTERED AT 10:11:40 ON 25 JUL 2005)

FILE 'REGISTRY' ENTERED AT 10:11:45 ON 25 JUL 2005

L1 STRUCTURE UPLOADED
L2 1 S L1
L3 33 S L1 FULL

FILE 'MEDLINE, BIOSIS, EMBASE, HCAPLUS, USPATFULL' ENTERED AT 10:12:28 ON 25 JUL 2005

L4 7 S L3
L5 7 DUP REM L4 (0 DUPLICATES REMOVED)
L6 267 S ANNEXIN? (P) ARTHRIT?
L7 53 S L6 AND PY<2000
L8 0 S ANNEXIN? AND ATHRIT? AND (CALCIUM INFLUX)
L9 26 S ARTHRIT? (P) (CALCIUM INFLUX)
L10 15 DUP REM L9 (11 DUPLICATES REMOVED)
L11 3922 S CALCIUM (P) ARTHRITIS
L12 64 S L11 (P) FLUX
L13 44 DUP REM L12 (20 DUPLICATES REMOVED)
L14 41 S L13 NOT L10

FILE 'MEDLINE, BIOSIS, EMBASE, CAPLUS' ENTERED AT 11:36:12 ON 25 JUL 2005

L15 22040 S CALCIUM INFLUX
L16 438 S L15 (P) INFLAMMAT?
L17 12 S L16 AND ARTHRITIS
L18 6 DUP REM L17 (6 DUPLICATES REMOVED)
L19 0 S L16 AND ANNEXIN

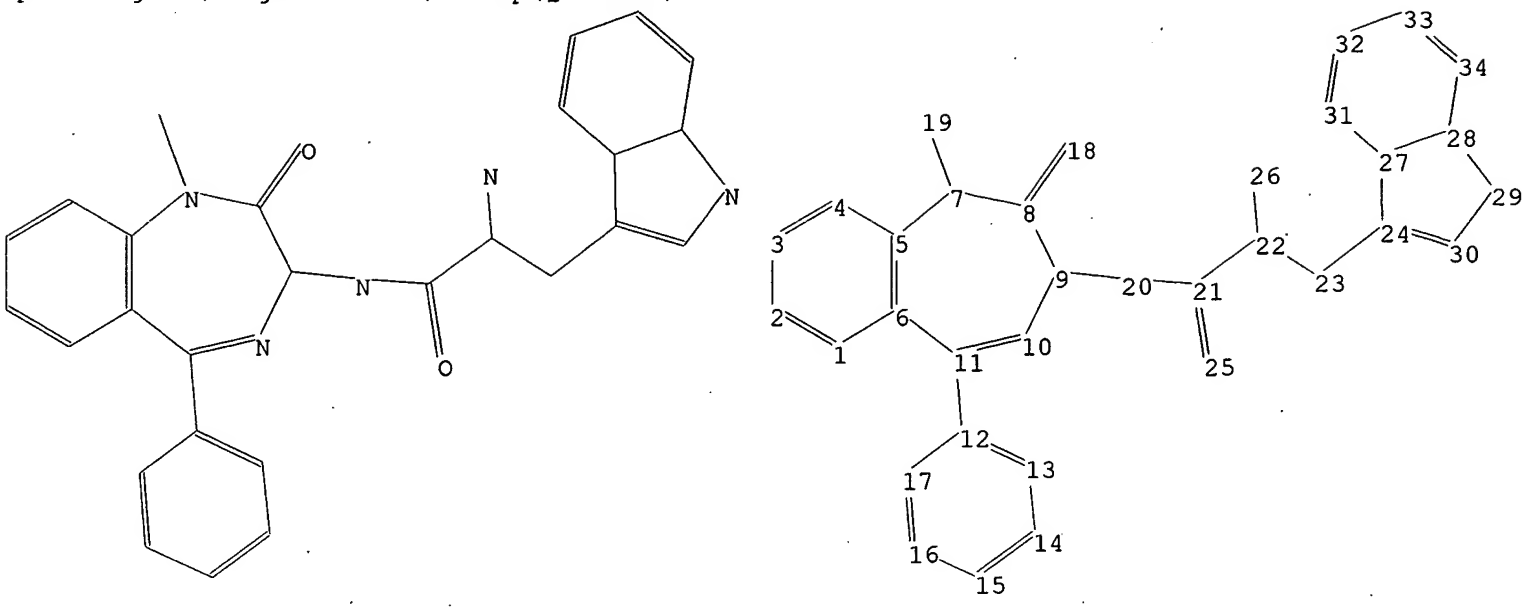
FILE 'REGISTRY' ENTERED AT 11:37:57 ON 25 JUL 2005

L20 99 S ANNEXIN V

FILE 'MEDLINE, BIOSIS, EMBASE, HCAPLUS' ENTERED AT 11:38:32 ON 25 JUL 2005

L21 14061 S L20 OR (ANNEXIN V)
L22 1134 S L21 AND INFLAMMAT?
L23 71 S L22 AND ARTHRITIS
L24 35 DUP REM L23 (36 DUPLICATES REMOVED)
L25 978 S L21 (P) INFLAMMAT?
L26 1 S L21 AND INFLAMMAT? AND (CALCIUM INFLUX)
L27 75 S L21 AND INFLAMMAT? AND CALCIUM
L28 3 S L27 AND ARTHRITIS
L29 2 DUP REM L28 (1 DUPLICATE REMOVED)
L30 16 S L27 AND PY<2000
L31 6 DUP REM L30 (10 DUPLICATES REMOVED)

Uploading C:\Program Files\Stnexp\Queries\10659801.str



chain nodes :
18 19 20 21 22 23 25 26
ring nodes :
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 24 27 28 29 30 31
32 33 34
chain bonds :
7-19 8-18 9-20 11-12 20-21 21-22 21-25 22-23 22-26 23-24
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-11 7-8 8-9 9-10 10-11 12-13 12-17 13-14
14-15 15-16 16-17 24-27 24-30 27-28 27-31 28-29 28-34 29-30 31-32 32-33 33-34
exact/norm bonds :
5-7 6-11 7-8 7-19 8-9 8-18 9-10 9-20 10-11 20-21 21-25 22-26 24-27 24-30
27-28 27-31 28-29 28-34 29-30 31-32 32-33 33-34
exact bonds :
11-12 21-22 22-23 23-24
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6 12-13 12-17 13-14 14-15 15-16 16-17

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:CLASS 19:CLASS 20:CLASS
21:CLASS
22:CLASS 23:CLASS 24:Atom 25:CLASS 26:CLASS 27:Atom 28:Atom 29:Atom 30:Atom 31:Atom
32:Atom
33:Atom 34:Atom

L1 STRUCTURE UPLOADED

L5 ANSWER 1 OF 7 USPATFULL on STN
AN 2004:70691 USPATFULL
TI Methods and compositions related to modulators of annexin and cartilage homeostasis
IN Chubinskaya, Susan, Vernon Hills, IL, UNITED STATES
Hutchins, Jeff, Chapel Hill, NC, UNITED STATES
Mollenhauer, Juergen, Eisenberg, GERMANY, FEDERAL REPUBLIC OF
Tavares, Francis X., Durham, NC, UNITED STATES
Thomson, Stephen A., Durham, NC, UNITED STATES
Worley, Jennings F., Durham, NC, UNITED STATES
PI US 2004053919 A1 20040318
AI US 2003-659801 A1 20030911 (10)
RLI Division of Ser. No. US 2000-745989, filed on 21 Dec 2000, GRANTED, Pat. No. US 6649366
PRAI US 1999-173692P 19991229 (60)
DT Utility
FS APPLICATION
LREP DAVID J LEVY, CORPORATE INTELLECTUAL PROPERTY, GLAXOSMITHKLINE, FIVE MOORE DR., PO BOX 13398, RESEARCH TRIANGLE PARK, NC, 27709-3398
CLMN Number of Claims: 28
ECL Exemplary Claim: 1
DRWN 3 Drawing Page(s)
LN.CNT 1477
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention provides a method of treating a subject with arthritis or an arthritic disease or preventing arthritis or arthritic disease in a subject, comprising administering to the subject a therapeutically effective amount of an agent that attenuates annexin function. Also provided are various methods of screening for agents and genes that increase collagen synthesis, decrease collagen degradation, or reduce or delay apoptosis, and methods of using the identified agents or nucleic acids for attaining or maintaining cartilage homeostasis, promoting cartilage repair, increasing collagen synthesis, decreasing collagen degradation, or reducing or delaying apoptosis. The invention also provides methods of decreasing mineralization of vesicles derived from chondrocytes and of promoting endochondral bone growth using agents that attenuates annexin function. The present invention also provides a composition comprising isolated chondrocytes, an agent that attenuates annexin function, and collagen fragments or other means for challenging chondrocytes, including for example, collagen fragments, collagen peptides, or immune mediators.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 2 OF 7 USPATFULL on STN
AN 2002:99457 USPATFULL
TI Methods and compositions related to modulators of annexin and cartilage homeostasis
IN Chubinskaya, Susan, Vernon Hills, IL, UNITED STATES
Hutchins, Jeff, Chapel Hill, NC, UNITED STATES
Mollenhauer, Juergen, Eisenberg, GERMANY, FEDERAL REPUBLIC OF
Tavares, Francis X., Durham, NC, UNITED STATES
Thomson, Stephen A., Durham, NC, UNITED STATES
Worley, Jennings F., Durham, NC, UNITED STATES
PI US 2002052358 A1 20020502
US 6649366 B2 20031118
AI US 2000-745989 A1 20001221 (9)
PRAI US 1999-173692P 19991229 (60)
DT Utility
FS APPLICATION
LREP DAVID J LEVY, VP INTELLECTUAL PROPERTY, GLAXO WELLCOME INC, GLOBAL INTELLECTUAL PROPERTY, FIVE MOORE DR, PO BOX 13398, RESEARCH TRIANGLE PARK, NC, 27709-3398
CLMN Number of Claims: 67
ECL Exemplary Claim: 1
DRWN 3 Drawing Page(s)
LN.CNT 1621

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention provides a method of treating a subject with arthritis or an arthritic disease or preventing arthritis or arthritic disease in a subject, comprising administering to the subject a therapeutically effective amount of an agent that attenuates annexin function. Also provided are various methods of screening for agents and genes that increase collagen synthesis, decrease collagen degradation, or reduce or delay apoptosis, and methods of using the identified agents or nucleic acids for attaining or maintaining cartilage homeostasis, promoting cartilage repair, increasing collagen synthesis, decreasing collagen degradation, or reducing or delaying apoptosis. The invention also provides methods of decreasing mineralization of vesicles derived from chondrocytes and of promoting endochondral bone growth using agents that attenuates annexin function. The present invention also provides a composition comprising isolated chondrocytes, an agent that attenuates annexin function, and collagen fragments or other means for challenging chondrocytes, including for example, collagen fragments, collagen peptides, or immune mediators.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 3 OF 7 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 2001:489222 HCAPLUS
DN 135:87192
TI Methods and compositions related to modulators of annexin and cartilage homeostasis
IN Chubinskaya, Susan; Hutchins, Jeff; Mollenhauer, Juergen; Tavares, Francis X.; Worley, Jennings F.; Thomson, Stephen A.
PA Glaxo Group Ltd., UK; Rush-Presbyterian St. Luke's Medical Center
SO PCT Int. Appl., 61 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001047510	A2	20010705	WO 2000-US34936	20001221
	WO 2001047510	A3	20020221		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	AU 2001027333	A5	20010709	AU 2001-27333	20001221
	US 2002052358	A1	20020502	US 2000-745989	20001221
	US 6649366	B2	20031118		
	EP 1244457	A2	20021002	EP 2000-990288	20001221
	EP 1244457	B1	20041027		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	JP 2003518494	T2	20030610	JP 2001-548105	20001221
	AT 280580	E	20041115	AT 2000-990288	20001221
	US 2004053919	A1	20040318	US 2003-659801	20030911
PRAI	US 1999-173692P	P	19991229		
	US 2000-745989	A3	20001221		
	WO 2000-US34936	W	20001221		

OS MARPAT 135:87192

AB The present invention provides a method of treating a subject with arthritis or an arthritic disease or preventing arthritis or arthritic disease in a subject, comprising administering to the subject a therapeutically effective amount of an agent that attenuates annexin function. Also provided are various methods of screening for agents and genes that increase collagen synthesis, decrease collagen degradation, or reduce or delay apoptosis, and methods of using the identified agents or

nucleic acids for attaining or maintaining cartilage homeostasis, promoting cartilage repair, increasing collagen synthesis, decreasing collagen degradation, or reducing or delaying apoptosis. The invention also provides methods of decreasing mineralization of vesicles derived from chondrocytes and of promoting endochondral bone growth using agents that attenuates annexin function. The present invention also provides a composition comprising isolated chondrocytes, an agent that attenuates annexin function, and collagen fragments or other means for challenging chondrocytes, including for example, collagen fragments, collagen peptides, or immune mediators. The claimed compds. for attenuation of annexin functions include 3-(R,S)-L-tryptophanyl-1,3-dihydro-1-methyl-5-phenyl-2H-1,4-benzodiazepine-2-one and 4-[3-[2-(4-benzyl)piperidinyl]propionyl]-7-methoxy-2,3,4,5-tetrahydro-1,4-benzothiazepine.

L5 ANSWER 4 OF 7 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 2001:846593 HCAPLUS
DN 136:256724
TI Peptide/benzodiazepine hybrids as ligands of CCKA and CCKB receptors
AU Escherich, Achim; Lutz, Jurgen; Escrieut, Chantal; Fourmy, Daniel; Van Neuren, A. Stephanie; Muller, Gerhard; Schafferhans, Andrea; Klebe, Gerhard; Moroder, Luis
CS Max-Planck Institute of Biochemistry, Martinsried, 82152, Germany
SO Biopolymers (2001), Volume Date 2000-2001, 56(2), 55-76
CODEN: BIPMAA; ISSN: 0006-3525
PB John Wiley & Sons, Inc.
DT Journal
LA English
AB The (neuro)hormones gastrin and cholecystokinin (CCK) share a common C-terminal tetrapeptide amide sequence that has been recognized as the message portion while the N-terminal extensions are responsible for the CCKA and CCKB receptor subtype selectivity and avidity. 1,4-Benzodiazepine derivs. are potent and selective antagonists of these receptors, and according to comparative mol. field anal., the structures of these nonpeptidic compds. could well mimic the message sequence of the peptide agonists at least in terms of spatial array of the aromatic residues. Docking of a larger series of low mol. weight nonpeptide antagonists to a homol. modeling derived CCKB receptor structure revealed a consensus binding mode that is further validated by data from site-directed mutagenesis studies of the receptors. Whether this putative binding pocket of the nonpeptide antagonists is identical to that of the message portion of the peptide agonists, or whether it is distinct and spatially separated, or overlapping, but with.
RE.CNT 90 THERE ARE 90 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 5 OF 7 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 2000:161321 HCAPLUS
DN 132:221336
TI Benzodiazepines and benzothiazepines derivatives and HBsAg peptides binding to annexins, their compositions and use
IN Depla, Erik; Moereels, Henri; Maertens, Geert
PA Innogenetics N.V., Belg.
SO PCT Int. Appl., 60 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2000012547	A2	20000309	WO 1999-EP6231	19990825
WO 2000012547	A3	20000615		

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

CA	2335102	AA	20000309	CA 1999-2335102	19990825
AU	9956247	A1	20000321	AU 1999-56247	19990825
BR	9913226	A	20010522	BR 1999-13226	19990825
EP	1107983	A2	20010620	EP 1999-942916	19990825
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP	2002525289	T2	20020813	JP 2000-571060	19990825
PRAI EP	1998-870186	A	19980901		
EP	1999-870062	A	19990329		
WO	1999-EP6231	W	19990825		

OS MARPAT 132:221336

AB The present invention relates to 1,4-benzodiazepines or 1,4-benzothiazepines derivatized with a peptide that can inhibit the interaction between annexin and annexin binding proteins. In particular, the present invention relates to 1,4-benzodiazepines or 1,4-benzothiazepines derivs. that can inhibit the interaction between annexin and viral proteins that bind annexins such as the HBsAg protein of HBV, glycoprotein B of the cytomegalovirus or any annexin binding protein from the influenza virus. These 1,4-benzodiazepines or 1,4-benzothiazepines derivs. can be used to prevent or treat diseases in which interactions between annexin family members and annexin binding proteins are involved such as HBV and/or HDV infections, cytomegalovirus infections or influenza virus infections.

L5 ANSWER 6 OF 7 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 2000:288376 HCAPLUS

DN 133:99693

TI Benzodiazepine/peptide hybrids as ligands for CCK-A and CCK-B receptors

AU Escherich, Achim; Lutz, Jurgen; Escrieut, Chantal; Fourmy, Daniel; Van Neuren, Stephanie; Muller, Gerhard; Moroder, Luis

CS Max-Planck-Institut fur Biochemie, Martinsried, 82152, Germany

SO Peptides 1998, Proceedings of the European Peptide Symposium, 25th, Budapest, Aug. 30-Sept. 4, 1998 (1999), Meeting Date 1998, 80-81. Editor(s): Bajusz, Sandor; Hudecz, Ferenc. Publisher: Akademiai Kiado, Budapest, Hung.
CODEN: 68WKAY

DT Conference

LA English

AB Results from mutational anal. studies of cholecystokinin-A (CCK-A) and cholecystokinin-B (CCK-B) receptors support different binding modes of non-peptidic and endogenous ligands, while comparative mol. field anal. studies of benzodiazepine-based antagonists and the message portion of the tetrapeptide amide hormones revealed surprising consistency. These previous studies inspired the authors' approach towards developing peptide/benzodiazepine hybrids in which the peptidic address was expected to dictate the binding mode of the Trp-benzodiazepine moieties as mimics of the message portion. A positional scanning of the peptide on various amine-functionalized benzodiazepines revealed that the constructs developed with 3-(R,S)-3-amino-1,3-dihydro-1-methyl-5-phenyl-2H-1,4-benzodiazepine-2-one (BDZ2) are recognized by CCK-A and CCK-B receptors as antagonists. Although the diastereomers related to the C3 of the benzodiazepine core were isolated in pure form for both the gastrin and cholecystokinin (CCK) hormone hybrids, unambiguous stereochem. assignment of the isomeric forms could not be achieved by NMR anal. The benzodiazepine derivative (S)-Devazepide is known to exhibit high preference for CCK-A (IC50 0.1 nM) vs. CCK-B receptor (IC50 0.1 μM) and the derivative (R)-L-365,260 for CCK-B (IC50 8.5 nM) vs. CCK-A receptor (IC50 0.74 μM). Similarly strong stereochem. restrictions as well as receptor affinities were not observed for the peptide/BDZ2 hybrids despite the structural homol. in the C-terminus. It can thus be concluded that the receptor binding sites of the benzodiazepine antagonists differ from those of the new hybrid constructs and that latter ligands may bind to the receptors in a mode similar to that of the endogenous hormones, although with significantly lower affinities.

RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 7 OF 7 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 1998:79073 HCAPLUS
DN 128:213221
TI Interactions of benzodiazepine derivatives with annexins
AU Hofmann, Andreas; Escherich, Achim; Lewit-Bentley, Anita; Benz, Jorg; Raguenes-Nicol, Celine; Russo-Marie, Francoise; Gerke, Volker; Moroder, Luis; Huber, Robert
CS Max-Planck-Institut fur Biochemie, Abt. Strukturforschung, Martinsried, D-82152, Germany
SO Journal of Biological Chemistry (1998), 273(5), 2885-2894
CODEN: JBCHA3; ISSN: 0021-9258
PB American Society for Biochemistry and Molecular Biology
DT Journal
LA English
AB Human annexins III and V, members of the annexin family of calcium- and membrane-binding proteins, were complexed within the protein crystals with BDA-452, a new 1,4-benzodiazepine derivative, by soaking and co-crystallization methods. The crystal structures of the complexes were analyzed by x-ray crystallog. and refined to 2.3- and 3.0-Å resolution BDA-452 binds to a cleft which is located close to the N-terminus opposite to the membrane-binding side of the proteins. Biophys. studies of the interactions of various benzodiazepine derivs. with annexins were performed to analyze the binding of benzodiazepines to annexins and their effects on the annexin-induced calcium influx into phosphatidylserine and phosphatidylethanolamine liposomes. Different effects were observed with a variety of benzodiazepines and different annexins depending on the ligand and protein. Almost opposite effects on annexin functions were elicited by BDA-250 and diazepam, its 7-chloro derivative Thus, benzodiazepines modulate the calcium influx activity of annexins allosterically by stabilizing or destabilizing the conducting state of peripherally bound annexins.
RE.CNT 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 1 OF 53 MEDLINE on STN
AN 1999414302 MEDLINE
DN PubMed ID: 10483027
TI Lymphocyte apoptosis in systemic lupus erythematosus: relationships with Fas expression, serum soluble Fas and disease activity.
AU Courtney P A; Crockard A D; Williamson K; McConnell J; Kennedy R J; Bell A L
CS Department of Rheumatology and Immunology, Royal Victoria Hospital, Belfast, Ireland.
SO Lupus, **(1999)** 8 (7) 508-13.
Journal code: 9204265. ISSN: 0961-2033.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199910
ED Entered STN: 19991101
Last Updated on STN: 19991101
Entered Medline: 19991020
AB Lupus specific autoantigens are exposed on apoptotic cells. The increased number of apoptotic lymphocytes reported in systemic lupus erythematosus (SLE) may be attributable to abnormalities of lymphocyte Fas expression or serum soluble Fas. In the present study we analysed the count of circulating apoptotic lymphocytes in SLE patients (n=50), by flow cytometry using **Annexin** V, compared to rheumatoid **arthritis** patients (RA, n=20), inflammatory bowel disease patients (IBD, n=20) and normal controls (n=20). Lymphocyte Fas expression and serum soluble Fas were measured and related to numbers of apoptotic lymphocytes. The percentage of apoptotic lymphocytes, determined by **Annexin** V binding, was significantly increased in peripheral blood of SLE patients (median=4.2%) compared with normal healthy donors (median=1.1%) and IBD patients (median=2. 0%) but not RA (median=3.9%). SLE lymphocyte Fas expression was not significantly different from RA or IBD patients. Serum soluble Fas in SLE patients correlated positively with apoptotic lymphocytes and antibodies to double stranded DNA. This study suggests that increased apoptotic lymphocytes and increased lymphocyte Fas expression may not be specific to SLE. Serum soluble Fas may have a role in the regulation of lymphocyte apoptosis in SLE.

L7 ANSWER 2 OF 53 MEDLINE on STN
AN 1999330077 MEDLINE
DN PubMed ID: 10403283
TI Inhibitory effect of **annexin** I on synovial inflammation in rat adjuvant **arthritis**.
AU Yang Y; Hutchinson P; Morand E F
CS Monash University, Melbourne, Victoria, Australia.
SO Arthritis and rheumatism, **(1999 Jul)** 42 (7) 1538-44.
Journal code: 0370605. ISSN: 0004-3591.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 199907
ED Entered STN: 19990730
Last Updated on STN: 19990730
Entered Medline: 19990720
AB OBJECTIVE: **Annexin** I is an endogenous antiinflammatory mediator, expressed in rheumatoid **arthritis** (RA) synovium, the contribution of which to autoregulation of the synovial inflammatory response has not been examined in models of RA. We investigated the antiinflammatory role of **annexin** I in rat adjuvant **arthritis**. METHODS: Rats with adjuvant-induced **arthritis** (AIA) were treated with a specific anti-**annexin** I monoclonal antibody (mAb), isotype control IgG, and/or dexamethasone. Clinical outcomes and synovial synthesis of tumor necrosis factor alpha (TNFalpha), prostaglandin E2 (PGE2), and nitric oxide were examined, and **annexin** I expression was assessed by flow cytometry and reverse

transcription-polymerase chain reaction. RESULTS: Anti-**annexin** I mAb reversed the effects of dexamethasone on the clinical features of AIA and exacerbated AIA in the absence of exogenous glucocorticoid. Clinical exacerbation of AIA by anti-**annexin** I mAb was accompanied by significantly increased synovial TNFalpha and PGE2, suggesting that **annexin** I tonically inhibits the production of these mediators. Anti-**annexin** I mAb treatment was associated with significantly reduced leukocyte intracellular **annexin** I, despite increased **annexin** I messenger RNA expression, consistent with a depletion effect of extracellular mAb via the cell surface. CONCLUSION: **Annexin** I is a key endogenous inhibitory mediator of **arthritis** via mechanisms that include inhibition of cytokine and effector molecule production. Moreover, a synthesis-independent depletion of intracellular **annexin** I by extracellular antibody supports the hypothesis that externalization of **annexin** I is involved in its mode of action.

L7 ANSWER 3 OF 53 MEDLINE on STN
AN 1999309041 MEDLINE
DN PubMed ID: 10225817
TI Increased apoptotic peripheral blood neutrophils in systemic lupus erythematosus: relations with disease activity, antibodies to double stranded DNA, and neutropenia.
AU Courtney P A; Crockard A D; Williamson K; Irvine A E; Kennedy R J; Bell A L
CS Department of Rheumatology, Musgrave Park Hospital, Stockman's Lane, Belfast BT9 7JB.
SO Annals of the rheumatic diseases, **(1999 May)** 58 (5) 309-14.
Journal code: 0372355. ISSN: 0003-4967.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199909
ED Entered STN: 19991005
Last Updated on STN: 19991005
Entered Medline: 19990917
AB OBJECTIVE: To quantify the percentage of apoptotic peripheral blood neutrophils in systemic lupus erythematosus (SLE) and to determine the relations with disease activity and neutropenia. METHODS: Neutrophil apoptosis in SLE patients (n =50) was assessed by flow cytometry using **annexin** V binding and fluorescent labelled anti-fas. Rheumatoid **arthritis** (RA, n =20) and inflammatory bowel disease patients (IBD, n =20) were studied as disease controls. RESULTS: The percentage of apoptotic neutrophils, determined by **annexin** V binding, was increased in peripheral blood of SLE patients (median = 3.25%) compared with normal healthy donors (n =20, median = 1.20%) and disease controls (RA: median = 1.15%) (IBD: median = 1.15%). SLE neutrophil apoptosis correlated positively with lupus disease activity measured by SLAM score. SLE patients with increased antibodies to dsDNA (>10 mg/ml) had increased apoptotic neutrophils. Eight of 14 neutropenic SLE patients had increased apoptotic neutrophils. Increased neutrophil fas expression compared with normal controls was observed in SLE, RA, and IBD. CONCLUSION: Neutrophil fas expression is increased non-specifically in inflammatory disease. Increased circulating apoptotic neutrophils in SLE correlate positively with disease activity (SLAM) and may contribute to autoantigen excess including dsDNA.

L7 ANSWER 4 OF 53 MEDLINE on STN
AN 1999047214 MEDLINE
DN PubMed ID: 9831319
TI Novel pathways for glucocorticoid effects on neutrophils in chronic inflammation.
AU Goulding N J; Euzger H S; Butt S K; Perretti M
CS Arthritis Research Section, St. Bartholomew's & Royal London School of Medicine & Dentistry, UK.
SO Inflammation research : official journal of the European Histamine Research Society ... [et al.], **(1998 Oct)** 47 Suppl 3 S158-65.

Ref: 68
Journal code: 9508160. ISSN: 1023-3830.
CY Switzerland
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 199902
ED Entered STN: 19990216
Last Updated on STN: 19990216
Entered Medline: 19990202
AB Neutrophils have been implicated in mediating much of the tissue damage associated with chronic inflammatory diseases such as rheumatoid **arthritis**, where they are involved in destruction of both cartilage and bone. Glucocorticoids are powerful anti-inflammatory agents, often used in the treatment of this autoimmune disease. They exert significant inhibitory effects on neutrophil activation and functions, such as chemotaxis, adhesion, transmigration, apoptosis, oxidative burst, and phagocytosis. The mechanisms by which glucocorticoids exert these effects on neutrophils are unclear. Evidence from studies of inflammation in human subjects and animal models suggests that **annexin**-I an endogenous, glucocorticoid-induced protein also known as lipocortin-1, has a pivotal role in modulating neutrophil activation, transmigratory, and phagocytic functions. Furthermore, we present evidence for altered neutrophil functions in rheumatoid **arthritis** that correspond to a significantly reduced capacity of these cells to bind **annexin**-I. A proposed novel pathway for glucocorticoid actions on neutrophils involving **annexin**-I could explain the development of chronic neutrophil activation in diseases such as rheumatoid **arthritis**.

L7 ANSWER 5 OF 53 MEDLINE on STN
AN 1998126053 MEDLINE
DN PubMed ID: 9466577
TI Synovial fibroblasts and the sphingomyelinase pathway: sphingomyelin turnover and ceramide generation are not signaling mechanisms for the actions of tumor necrosis factor-alpha.
AU Gerritsen M E; Shen C P; Perry C A
CS Institute for Bone and Joint Disease and Cancer, Bayer Corporation, West Haven, Connecticut, USA.. meg@gene.com
SO American journal of pathology, **(1998 Feb)** 152 (2) 505-12.
Journal code: 0370502. ISSN: 0002-9440.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 199803
ED Entered STN: 19980319
Last Updated on STN: 19980319
Entered Medline: 19980306
AB The activation of sphingomyelinase and the generation of ceramide has been proposed to mediate tumor necrosis factor-alpha (TNF-alpha)-induced nuclear factor (NF)-kappaB activation through its second messenger ceramide. Ceramide may also be an important regulator of cell growth, senescence, and apoptosis. Aberrant cell proliferation and apoptosis have been implicated in the rampant fibroblast proliferation and pannus formation characteristic of rheumatoid **arthritis**. However, the role of TNF-alpha and the sphingomyelinase pathway in the process have not been determined. The objective of this study was to determine whether TNF-alpha activates the sphingomyelin pathway in human synovial fibroblasts (HSF) and the potential role of ceramide in HSF proliferation and apoptosis. Cultured human synovial fibroblasts were stimulated with exogenous TNF-alpha, sphingomyelinase, and ceramide. Apoptosis was assessed by cell morphology and **annexin** V labeling. NF-kappaB and stress kinase pathway activation were determined by immunoblotting techniques. Sphingomyelinase activation was determined by quantitation of sphingomyelin and ceramide radioactivity in [14C]serine-prelabeled HSF

cells. The addition of TNF-alpha (50 ng/ml) to HSF did not elicit detectable sphingomyelinase activation. TNF-alpha was shown to activate NF-kappaB (p65 translocation and degradation of IkappaBalpha) and the stress kinase pathway (phosphorylation of ATF-2, p38, and c-jun). In contrast, exogenous ceramide had no effect on these signaling pathways nor did ceramide stimulate the generation of interleukin-6 or interleukin-8. High concentrations of ceramide (> or =25 micromol/L) were cytotoxic, whereas lower concentrations of ceramide inhibited cell cycle progression. Thus, although TNF-alpha stimulates the NF-kappaB and stress kinase pathways in HSF, these effects of TNF-alpha are not associated with sphingomyelinase turnover or induction of apoptosis.

L7 ANSWER 6 OF 53 MEDLINE on STN
AN 97374486 MEDLINE
DN PubMed ID: 9230935
TI Annexins in cancer and autoimmune diseases.
AU Bastian B C
CS Klinik und Poliklinik fur Hautkrankheiten, Julius-Maximilians Universitat Wurzburg, Germany.
SO Cellular and molecular life sciences : CMLS, **(1997 Jun)** 53 (6) 554-6. Ref: 44
Journal code: 9705402. ISSN: 1420-682X.
CY Switzerland
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LA English
FS Priority Journals
EM 199708
ED Entered STN: 19970825
Last Updated on STN: 19970825
Entered Medline: 19970814
AB Several **annexins** have been implicated in the pathogenesis of benign and malignant neoplasms of different origins. In some tumours a suppressive action of **annexins** has been shown, whereas studies of other tumours indicate an involvement of **annexins** in tumour progression. In the light of the expression of **annexins** at distinct episodes of fetal development these observations point towards a functional role of **annexins** in cellular development and differentiation. This view is supported by data that link certain **annexins** to distinct pathways of signal transduction.
Auto-antibodies against several **annexins** have been detected in patients with autoimmune diseases such as systemic lupus erythematosus, rheumatoid **arthritis** and inflammatory bowel disease. Until now it is unclear whether their presence reflects a relevant pathogenetic mechanism or merely represents an unspecific expression of a raised autoimmunity in these patients.

L7 ANSWER 7 OF 53 MEDLINE on STN
AN 97166894 MEDLINE
DN PubMed ID: 9014583
TI **Annexin** V autoantibodies in rheumatoid **arthritis**.
AU Rodriguez-Garcia M I; Fernandez J A; Rodriguez A; Fernandez M P; Gutierrez C; Torre-Alonso J C
CS Department of Biochemistry and Molecular Biology, Faculty of Medicine, University of Oviedo, Spain.
SO Annals of the rheumatic diseases, **(1996 Dec)** 55 (12) 895-900.
Journal code: 0372355. ISSN: 0003-4967.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199702
ED Entered STN: 19970305
Last Updated on STN: 19970305
Entered Medline: 19970219
AB OBJECTIVE: To investigate the occurrence of anti-**annexin** V autoantibodies in sera of patients with rheumatoid **arthritis** to assess involvement with the disease and any relation to glucocorticoid

treatment. METHODS: Anti-**annexin** V antibodies were measured by an enzyme linked immunosorbent assay (ELISA) which used the purified human recombinant protein as antigen. RESULTS: Concentrations of anti-**annexin** V autoantibodies, predominantly of the IgG class, were significantly raised in sera from patients with rheumatoid **arthritis** compared to normal controls. This was not correlated with other indices of disease activity such as erythrocyte sedimentation rate or C reactive protein and was unrelated to glucocorticoid treatment. CONCLUSIONS: Extracellular **annexin** V provides an antigenic stimulus for autoantibody production and its in vivo expression is independent of glucocorticoid control. Such autoantibodies may have a detrimental role in the **arthritic** condition by interfering with putative functions of **annexin** V, including collagen type II binding, inhibition of phospholipase A2 activity, and Fc receptor activity.

L7 ANSWER 8 OF 53 MEDLINE on STN
AN 96097727 MEDLINE
DN PubMed ID: 7492225
TI Differential distribution of annexins-I, -II, -IV, and -VI in synovium.
AU Goulding N J; Dixey J; Morand E F; Dodds R A; Wilkinson L S; Pitsillides A A; Edwards J C
CS Medical College of St. Bartholomew's Hospital, London, United Kingdom.
SO Annals of the rheumatic diseases, **(1995 Oct)** 54 (10) 841-5.
Journal code: 0372355. ISSN: 0003-4967.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199601
ED Entered STN: 19960125
Last Updated on STN: 19960125
Entered Medline: 19960104
AB OBJECTIVES--To examine the distribution of four **annexins** in non-inflamed rheumatoid **arthritic** and osteoarthritic synovial tissue. METHODS--Frozen sections were stained with monoclonal antibodies (MAb) specific for **annexins**-I, -II, -IV, and -VI, and for cell lineage related markers including CD68 and CD14 (macrophages), prolyl hydroxylase (fibroblasts), and CD3 (T cells). RESULTS--Each of the **annexins** was present in synovial tissues in significant amounts in the three groups studied. **Annexin**-I was predominantly found within the synovial lining layer and double labelling showed it to be present predominantly in cells of the macrophage lineage. In rheumatoid specimens there was increased staining within the lining layer, perivascularly and on macrophages within the tissue stroma. **Annexin**-II was present in a distribution similar to that of **annexin**-I, but with more prominent perivascular staining. **Annexins**-IV and -VI were seen chiefly in association with areas of lymphocyte infiltration in rheumatoid tissue, whereas **annexins**-I and -II were absent from these areas. Endothelial cells stained weakly positive for **annexins**-I and -II, and more strongly for -IV and -VI. CONCLUSIONS--This study demonstrates that **annexins** (particularly **annexin**-I, a putative mediator of the anti-inflammatory activities of glucocorticoids) are abundant in rheumatoid and non-rheumatoid synovial tissue, **annexins**-IV and -VI having a distribution distinct from that of -I and -II.

L7 ANSWER 9 OF 53 MEDLINE on STN
AN 96057274 MEDLINE
DN PubMed ID: 7562750
TI High levels of antibodies to **annexins** V and VI in patients with rheumatoid **arthritis**.
AU Dubois T; Bisagni-Faure A; Coste J; Mavoungou E; Menkes C J; Russo-Marie F; Rothhut B
CS Laboratoire de Signalisation, Inflammation et Transformation Cellulaire, INSERM U.332, Institut Cochin de Genetique Moleculaire (ICGM), Universite Rene Descartes, Paris, France.
SO Journal of rheumatology, **(1995 Jul)** 22 (7) 1230-4.

Journal code: 7501984. ISSN: 0315-162X.
CY Canada
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199511
ED Entered STN: 19951227
Last Updated on STN: 19951227
Entered Medline: 19951122
AB OBJECTIVE. Glucocorticoids are powerful antiinflammatory agents widely used for the treatment of rheumatoid **arthritis** (RA). Synthesis and/or secretion of **annexin** I (A-I) is induced by these steroids. **Annexins** V and VI are also found extracellularly but are not induced by glucocorticoids. **Annexins** may be potent antagonists of phospholipase A2 (PLA2). Since autoantibodies to A-I have been reported in patients with RA, we studied the reactivity of sera from patients with RA to A-V and A-VI. METHODS. Sera from 26 patients with RA were assessed for anti-A-V and anti-A-VI antibodies and compared with sera from 26 sex/age matched healthy subjects. IgG and IgM antibodies were analyzed in an ELISA. A correlation study with disease activity and corticosteroid treatment schedule was performed. RESULTS. Sera from patients with RA contained significantly higher levels of IgG [anti-A-V and anti-A-VI] autoantibodies than control sera, both being correlated. This rise in antiannexin antibody titers was correlated with the RA activity score, and negatively correlated with the daily dose of corticosteroids. CONCLUSION. High levels of IgG (anti-A-V and anti-A-VI) antibodies were found in sera from patients with RA. We suggest that antiannexin autoantibodies may play a role in the clinical course of RA by impairing the anti-PLA2 effect of **annexins**.

L7 ANSWER 10 OF 53 MEDLINE on STN
AN 95214061 MEDLINE
DN PubMed ID: 7699691
TI Prevalence and characteristics of anti-56K/annexin XI autoantibodies in systemic autoimmune diseases.
AU Misaki Y; Van Venrooij W J; Pruijn G J
CS Department of Biochemistry, University of Nijmegen, The Netherlands.
SO Journal of rheumatology, **(1995 Jan)** 22 (1) 97-102.
Journal code: 7501984. ISSN: 0315-162X.
CY Canada
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199505
ED Entered STN: 19950510
Last Updated on STN: 19950510
Entered Medline: 19950503
AB OBJECTIVE. To investigate the occurrence and features of anti-56K/**annexin** XI autoantibodies in sera from patients with various systemic autoimmune diseases, including rheumatoid **arthritis**, systemic lupus erythematosus, Sjogren's syndrome, systemic sclerosis, polymyositis and Raynaud's phenomenon. METHODS. Anti-56K/**annexin** XI autoantibodies were detected by an enzyme linked immunosorbent assay using the bacterially expressed recombinant protein as antigen. RESULTS. Anti-56K/**annexin** XI autoantibodies were found in a substantial number of patient sera (4.1-10.1%), but are rarely detected in sera from healthy controls and from patients with infectious diseases. Disease specificity was not observed. The majority of these autoantibodies belong to the IgG class and their titers in positive sera are at least as high as those of other well defined autoantibodies. CONCLUSION. Anti-56K/**annexin** XI autoantibodies frequently occur in systemic autoimmune diseases in contrast to infectious diseases and healthy individuals and are primarily of the IgG isotype, consistent with an antigen driven mechanism of autoantibody production.

L7 ANSWER 11 OF 53 MEDLINE on STN
AN 95169666 MEDLINE
DN PubMed ID: 7865477

TI Autoantibodies to annexins: a diagnostic marker for cutaneous disorders?.
AU Bastian B C; Nuss B; Romisch J; Kraus M; Brocker E B
CS Department of Dermatology, University of Wurzburg, Germany.
SO Journal of dermatological science, **(1994 Dec)** 8 (3) 194-202.
Journal code: 9011485. ISSN: 0923-1811.
CY Ireland
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199503
ED Entered STN: 19950407
Last Updated on STN: 19950407
Entered Medline: 19950330
AB **Annexins**/lipocortins are a group of structurally related calcium and lipid binding proteins which have been implicated as mediators of the anti-inflammatory action of corticosteroids. Autoantibodies against **annexin**-1 have been reported in association with autoimmune diseases such as systemic lupus erythematosus and rheumatoid **arthritis** and their presence has been hypothesized as the reason for the steroid resistance phenomenon. In this study we investigated IgG- and IgM-autoantibodies against **annexin**-1,-2,-3,-4,-5 and -6 in sera of 221 patients with skin disorders and 114 healthy blood donors with newly established ELISAs. Patients were clustered into 5 groups according to their diagnosis: autoimmune diseases, psoriasis, leg ulcer, malignant melanoma, and miscellaneous diseases. Autoantibodies directed against each **annexin** were detectable in all investigated groups, in the control group as well as in the disease groups, without displaying any significant correlation to any of the disease states. The homogenous distribution of **annexin**-autoantibodies throughout the control group and all the disease groups studied, do not support the implication of **annexin**-autoantibodies in pathophysiological states and make them an unlikely candidate for use as a diagnostic marker.

L7 ANSWER 12 OF 53 MEDLINE on STN
AN 94140847 MEDLINE
DN PubMed ID: 7508441
TI The 56K autoantigen is identical to human annexin XI.
AU Misaki Y; Pruijn G J; van der Kemp A W; van Venrooij W J
CS Department of Biochemistry, University of Nijmegen, The Netherlands.
SO Journal of biological chemistry, **(1994 Feb 11)** 269 (6) 4240-6.
Journal code: 2985121R. ISSN: 0021-9258.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
OS GENBANK-L19605
EM 199403
ED Entered STN: 19940330
Last Updated on STN: 19960129
Entered Medline: 19940317
AB Anti-56K autoantibodies are present in sera from patients with various autoimmune diseases, predominantly in sera from patients with rheumatoid **arthritis**, systemic lupus erythematosus, or Sjogren's syndrome. To clarify the molecular structure of this autoantigen, we isolated a 2.0-kilobase pair cDNA clone considered to encode the full-length 56K autoantigen. The longest open reading frame encodes a 505-amino acid polypeptide, with a predicted molecular mass of 54.4 kDa. The in vitro translated protein is recognized by all anti-56K positive patient sera tested. Antibodies affinity-purified using the bacterially expressed recombinant protein recognized the 56K autoantigen in a HeLa cell extract. cDNA sequencing revealed that the 56K cDNA shares a high degree of homology in both nucleotide (87%) and amino acid sequence (92.5%) with bovine **annexin** XI, indicating that the 56K cDNA encodes the human homologue of **annexin** XI, a member of the Ca(2+)-dependent phospholipid binding protein family. Anti-56K autoantibody exhibits both a cytoplasmic and a nuclear staining in immunofluorescence experiments. Patients' sera recognize preferentially the N-terminal region of the protein, which is specific for 56K/**annexin** XI and not shared by

other **annexins**, indicating that the autoimmune response to 56K/ **annexin** XI in these patients is specific for this **annexin** family member.

L7 ANSWER 13 OF 53 MEDLINE on STN
AN 93075349 MEDLINE
DN PubMed ID: 1445462
TI Specific binding of lipocortin-1 (**annexin** I) to monocytes and neutrophils is decreased in rheumatoid **arthritis**.
AU Goulding N J; Jefferiss C M; Pan L; Rigby W F; Guyre P M
CS Bath Institute for Rheumatic Diseases, UK.
NC AI-19053 (NIAID)
CA-23108 (NCI)
DK-33100 (NIDDK)
SO Arthritis and rheumatism, **(1992 Nov)** 35 (11) 1395-7.
Journal code: 0370605. ISSN: 0004-3591.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 199212
ED Entered STN: 19930122
Last Updated on STN: 19930122
Entered Medline: 19921207

L7 ANSWER 14 OF 53 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
AN 1999:528295 BIOSIS
DN PREV199900528295
TI Lymphocyte apoptosis in systemic lupus erythematosus: Relationships with Fas expression, serum soluble Fas and disease activity.
AU Courtney, P. A. [Reprint author]; Crockard, A. D.; Williamson, K.; McConnell, J.; Kennedy, R. J.; Bell, A. L.
CS Department of Rheumatology and Immunology, Musgrove Park Hospital, Stockman's Lane, Belfast, BT0 7JB, UK
SO Lupus, (1999) Vol. 8, No. 7, pp. 508-513. print.
ISSN: 0961-2033.
DT Article
LA English
ED Entered STN: 10 Dec 1999
Last Updated on STN: 10 Dec 1999
AB Lupus specific autoantigens are exposed on apoptotic cells. The increased number of apoptotic lymphocytes reported in systemic lupus erythematosus (SLE) may be attributable to abnormalities of lymphocyte Fas expression or serum soluble Fas. In the present study we analysed the count of circulating apoptotic lymphocytes in SLE patients (n = 50), by flow cytometry using **Annexin** V, compared to rheumatoid **arthritis** patients (RA, n = 20), inflammatory bowel disease patients (IBD, n = 20) and normal controls (n = 20). Lymphocyte Fas expression and serum soluble Fas were measured and related to numbers of apoptotic lymphocytes. The percentage of apoptotic lymphocytes, determined by **Annexin** V binding, was significantly increased in peripheral blood of SLE patients (median = 4.2%) compared with normal healthy donors (median = 1.1%) and IBD patients (median = 2.0%) but not RA (median = 3.9%). SLE lymphocyte Fas expression was not significantly different from RA or IBD patients. Serum soluble Fasin SLE patients correlated positively with apoptotic lymphocytes and antibodies to double stranded DNA. This study suggests that increased apoptotic lymphocytes and increased lymphocyte Fas expression may not be specific to SLE. Serum soluble Fas may have a role in the regulation of lymphocyte apoptosis in SLE.

L7 ANSWER 15 OF 53 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
AN 1999:389025 BIOSIS
DN PREV199900389025
TI Inhibitory effect of **annexin** I on synovial inflammation in rat adjuvant **arthritis**.

AU Yang, Yuanhang; Hutchinson, Paul; Morand, Eric F. [Reprint author]
CS Centre for Inflammatory Diseases, Department of Medicine, Monash Medical Centre, Monash University, Melbourne, Victoria, 3168, Australia
SO Arthritis and Rheumatism, (July, 1999) Vol. 42, No. 7, pp. 1538-1544. print.
CODEN: ARHEAW. ISSN: 0004-3591.
DT Article
LA English
ED Entered STN: 28 Sep 1999
Last Updated on STN: 28 Sep 1999
AB Objective. **Annexin** I is an endogenous antiinflammatory mediator, expressed in rheumatoid **arthritis** (RA) synovium, the contribution of which to autoregulation of the synovial inflammatory response has not been examined in models of RA. We investigated the antiinflammatory role of **annexin** I in rat adjuvant **arthritis**. Methods. Rats with adjuvant-induced **arthritis** (AIA) were treated with a specific anti-**annexin** I monoclonal antibody (mAb), isotype control IgG, and/or dexamethasone. Clinical outcomes and synovial synthesis of tumor necrosis factor alpha (TNFalpha), prostaglandin E2 (PGE2), and nitric oxide were examined, and **annexin** I expression was assessed by flow cytometry and reverse transcription-polymerase chain reaction. Results. Anti-**annexin** I mAb reversed the effects of dexamethasone on the clinical features of AIA and exacerbated AIA in the absence of exogenous glucocorticoid. Clinical exacerbation of AIA by anti-**annexin** I mAb was accompanied by significantly increased synovial TNFalpha and PGE2, suggesting that **annexin** I tonically inhibits the production of these mediators. Anti-**annexin** I mAb treatment was associated with significantly reduced leukocyte intracellular **annexin** I, despite increased **annexin** I messenger RNA expression, consistent with a depletion effect of extracellular mAb via the cell surface. Conclusion. **Annexin** I is a key endogenous inhibitory mediator of **arthritis** via mechanisms that include inhibition of cytokine and effector molecule production. Moreover, a synthesis-independent depletion of intracellular **annexin** I by extracellular antibody supports the hypothesis that externalization of **annexin** I is involved in its mode of action.

L7 ANSWER 16 OF 53 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
AN 1999:278651 BIOSIS
DN PREV199900278651
TI Increased apoptotic peripheral blood neutrophils in systemic lupus erythematosus: Relations with disease activity, antibodies to double stranded DNA, and neutropenia.
AU Courtney, P. A. [Reprint author]; Crockard, A. D.; Williamson, K.; Irvine, A. E.; Kennedy, R. J.; Bell, A. L.
CS Department of Rheumatology, Musgrave Park Hospital, Stockman's Lane, Belfast, BT9 7JB, UK
SO Annals of the Rheumatic Diseases, (May, 1999) Vol. 58, No. 5, pp. 309-314. print.
CODEN: ARDIAO. ISSN: 0003-4967.
DT Article
LA English
ED Entered STN: 28 Jul 1999
Last Updated on STN: 28 Jul 1999
AB Objective-To quantify the percentage of apoptotic peripheral blood neutrophils in systemic lupus erythematosus (SLE) and to determine the relations with disease activity and neutropenia. Methods-Neutrophil apoptosis in SLE patients (n = 50) was assessed by flow cytometry using **annexin** V binding and fluorescent labelled anti-fas. Rheumatoid **arthritis** (RA, n = 20) and inflammatory bowel disease patients (IBD, n =20) were studied as disease controls. Results-The percentage of apoptotic neutrophils, determined by **annexin** V binding, was increased in peripheral blood of SLE patients (median = 3.25%) compared with normal healthy donors (n = 20, median = 1.20%) and disease controls (RA: median = 1.15%) (IBD: median = 1.15%). SLE neutrophil apoptosis correlated positively with lupus disease activity measured by SLAM score.

SLE patients with increased antibodies to dsDNA (>10 mg/ml) had increased apoptotic neutrophils. Eight of 14 neutropenic SLE patients had increased apoptotic neutrophils. Increased neutrophil fas expression compared with normal controls was observed in SLE, RA, and IBD. Conclusion-Neutrophil fas expression is increased non-specifically in inflammatory disease. Increased circulating apoptotic neutrophils in SLE correlate positively with disease activity (SLAM) and may contribute to autoantigen excess including dsDNA.

L7 ANSWER 17 OF 53 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
AN 1998:468769 BIOSIS
DN PREV199800468769
TI **Annexin** I: A constitutive inhibitory regulator of synovial inflammation in rat adjuvant **arthritis**.
AU Yang, Yuanhang; Hutchinson, Paul; Morand, Eric F.
CS Monash Univ., Melbourne, Australia
SO Arthritis and Rheumatism, (Sept., 1998) Vol. 41, No. 9 SUPPL., pp. S97. print.
Meeting Info.: 62nd National Scientific Meeting of the American College of Rheumatology and the 33rd National Scientific Meeting of the Association of Rheumatology Health Professionals. San Diego, California, USA. November 8-12, 1998. American College of Rheumatology; Association of Rheumatology Health Professionals.
CODEN: ARHEAW. ISSN: 0004-3591.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
Conference; (Meeting Poster)
LA English
ED Entered STN: 30 Oct 1998
Last Updated on STN: 30 Oct 1998

L7 ANSWER 18 OF 53 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
AN 1998:134307 BIOSIS
DN PREV199800134307
TI Synovial fibroblasts and the sphingomyelinase pathway: Sphingomyelin turnover and ceramide generation are not signaling mechanisms for the actions of tumor necrosis factor-alpha.
AU Gerritsen, Mary E. [Reprint author]; Shen, Chien-Ping; Perry, Carol A.
CS Genentech, One DNA Way, MS 42, South San Francisco, CA 94080, USA
SO American Journal of Pathology, (Feb., 1998) Vol. 152, No. 2, pp. 505-512. print.
CODEN: AJPAA4. ISSN: 0002-9440.
DT Article
LA English
ED Entered STN: 20 Mar 1998
Last Updated on STN: 20 Mar 1998
AB The activation of sphingomyelinase and the generation of ceramide has been proposed to mediate tumor necrosis factor-alpha (TNF-alpha)-induced nuclear factor (NF)-kappaB activation through its second messenger ceramide. Ceramide may also be an important regulator of cell growth, senescence, and apoptosis. Aberrant cell proliferation and apoptosis have been implicated in the rampant fibroblast proliferation and pannus formation characteristic of rheumatoid **arthritis**. However, the role of TNF-alpha and the sphingomyelinase pathway in the process have not been determined. The objective of this study was to determine whether TNF-alpha activates the sphingomyelin pathway in human synovial fibroblasts (HSF) and the potential role of ceramide in HSF proliferation and apoptosis. Cultured human synovial fibroblasts were stimulated with exogenous TNF-alpha, sphingomyelinase, and ceramide. Apoptosis was assessed by cell morphology and **annexin** V labeling. NF-kappaB and stress kinase pathway activation were determined by immunoblotting techniques. Sphingomyelinase activation was determined by quantitation of sphingomyelin and ceramide radioactivity in (14C)serine-prelabeled HSF cells. The addition of TNF-alpha (50 ng/ml) to HSF did not elicit detectable sphingomyelinase activation. TNF-alpha was shown to activate NF-kappaB (p65 translocation and degradation of IkappaBalpha) and the

stress kinase pathway (phosphorylation of ATF-2, p38, and c-jun). in contrast, exogenous ceramide had no effect on these signaling pathways nor did ceramide stimulate the generation of interleukin-6 or interleukin-8. High concentrations of ceramide (gtoreq25 mumol/L) were cytotoxic, whereas lower concentrations of ceramide inhibited cell cycle progression. Thus, although TNF-alpha stimulates the NF-kappaB and stress kinase pathways in HSF, these effects of TNF-alpha are not associated with sphingomyelinase turnover or induction of apoptosis.

L7 ANSWER 19 OF 53 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
AN 1997:361856 BIOSIS
DN PREV199799653789
TI Annexins in cancer and autoimmune diseases.
AU Bastian, B. C.
CS Cancer Genetics Program, Univ. California San Francisco, Cancer Cent., Box 0808, San Francisco, CA 94143-0808, USA
SO CMLS Cellular and Molecular Life Sciences, (1997) Vol. 53, No. 6, pp. 554-556.
ISSN: 1420-682X.
DT Article
General Review; (Literature Review)
LA English
ED Entered STN: 25 Aug 1997
Last Updated on STN: 25 Aug 1997
AB Several **annexins** have been implicated in the pathogenesis of benign and malignant neoplasms of different origins. In some tumours a suppressive action of **annexins** has been shown, whereas studies of other tumours indicate an involvement of **annexins** in tumour progression. In the light of the expression of **annexins** at distinct episodes of fetal development these observations point towards a functional role of **annexins** in cellular development and differentiation. This view is supported by data that link certain **annexins** to distinct pathways of signal transduction. Auto-antibodies against several **annexins** have been detected in patients with autoimmune diseases such as systemic lupus erythematosus, rheumatoid **arthritis** and inflammatory bowel disease. Until now it is unclear whether their presence reflects a relevant pathogenetic mechanism or merely represents an unspecific expression of a raised autoimmunity in these patients.

L7 ANSWER 20 OF 53 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
AN 1997:66144 BIOSIS
DN PREV199799365347
TI **Annexin** V autoantibodies in rheumatoid **arthritis**.
AU Rodriguez-Garcia, M. I.; Fernandez, J. A.; Rodriguez, A.; Fernandez, M. P.; Gutierrez, C.; Torre-Alonso, J. C. [Reprint author]
CS Dep. Biochem. and Molecular Biol., Fac. Med., Univ. Oviedo, E-330006 Oviedo, Spain
SO Annals of the Rheumatic Diseases, (1996) Vol. 55, No. 12, pp. 895-900.
CODEN: ARDIAO. ISSN: 0003-4967.
DT Article
LA English
ED Entered STN: 11 Feb 1997
Last Updated on STN: 11 Feb 1997
AB Objective-To investigate the occurrence of anti-**annexin** V autoantibodies in sera of patients with rheumatoid **arthritis** to assess involvement with the disease and any relation to glucocorticoid treatment. Methods-Anti-**annexin** V antibodies were measured by an enzyme linked immunosorbent assay (ELISA) which used the purified human recombinant protein as antigen. Results-Concentrations of anti-**annexin** V autoantibodies, predominantly of the IgG class, were significantly raised in sera from patients with rheumatoid **arthritis** compared to normal controls. This was not correlated with other indices of disease activity such as erythrocyte sedimentation rate or C reactive protein and was unrelated to glucocorticoid treatment. Conclusions-Extracellular **annexin** V provides an antigenic

stimulus for autoantibody production and its in vivo expression is independent of glucocorticoid control. Such autoantibodies may have a detrimental role in the **arthritic** condition by interfering with putative functions of **annexin** V, including collagen type II binding, inhibition of phospholipase A-2 activity, and Fc receptor activity.

L7 ANSWER 21 OF 53 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
AN 1995:549234 BIOSIS
DN PREV199698563534
TI Differential distribution of annexins-I, -II, -IV, and -VI in synovium.
AU Goulding, N. J. [Reprint author]; Dixey, J.; Morand, E. F.; Dodds, R. A.; Wilkinson, L. S.; Pitsillides, A. A.; Edwards, J. C. W.
CS Dep. Rheumatol., Med. Coll. St. Bartholomew's Hosp., Charterhouse Square, London EC1M 6BQ, UK
SO Annals of the Rheumatic Diseases, (1995) Vol. 54, No. 10, pp. 841-845. CODEN: ARDIAO. ISSN: 0003-4967.
DT Article
LA English
ED Entered STN: 31 Dec 1995
Last Updated on STN: 31 Dec 1995
AB Objectives: To examine the distribution of four **annexins** in non-inflamed rheumatoid **arthritic** and osteoarthritic synovial tissue. Methods: Frozen sections were stained with monoclonal antibodies (MAb) specific for **annexins**-I, -II, -IV, and -VI, and for cell lineage related markers including CD68 and CD14 (macrophages), prolyl hydroxylase (fibroblasts), and CD3 (T cells). Results: Each of the **annexins** was present in synovial tissues in significant amounts in the three groups studied. **Annexin**-I was predominantly found within the synovial lining layer and double labelling showed it to be present predominantly in cells of the macrophage lineage. In rheumatoid specimens there was increased staining within the lining layer, perivascularly and on macrophages within the tissue stroma. **Annexin**-II was present in a distribution similar to that of **annexin**-I, but with more prominent perivascular staining. **Annexins**-IV and -VI were seen chiefly in association with areas of lymphocyte infiltration in rheumatoid tissue, whereas **annexins**-I and -II were absent from these areas. Endothelial cells stained weakly positive for **annexins**-I and -II, and more strongly for -IV and -VI. Conclusions-This study demonstrates that, **annexins** (particularly **annexin**-I, a putative mediator of the anti-inflammatory activities of glucocorticoids) are abundant in rheumatoid and non-rheumatoid synovial tissue, **annexins** -IV and -VI having a distribution distinct from that of -I and -II.

L7 ANSWER 22 OF 53 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
AN 1995:409657 BIOSIS
DN PREV199598423957
TI High levels of antibodies to **annexins** V and VI in patients with rheumatoid **arthritis**.
AU Dubois, Thierry [Reprint author]; Bisagni-Faure, Anne; Coste, Joel; Mavoungou, Elie; Menkes, Charles-Joel; Russo-Marie, Francoise; Rothhut, Bernard
CS INSERM U.332, ICGM, 22 Rue Mechain, 75014 Paris, France
SO Journal of Rheumatology, (1995) Vol. 22, No. 7, pp. 1230-1234. CODEN: JRHUA9. ISSN: 0315-162X.
DT Article
LA English
ED Entered STN: 27 Sep 1995
Last Updated on STN: 27 Sep 1995
AB Objective: Glucocorticoids are powerful antiinflammatory agents widely used for the treatment of rheumatoid **arthritis** (RA). Synthesis and/or secretion of **annexin** I (A-I) is induced by these steroids. **Annexins** V and VI are also found extracellularly but are not induced by glucocorticoids. **Annexins** may be potent antagonists of phospholipase A-2 (PLA-2). Since autoantibodies to A-I

have been reported in patients with RA, we studied the reactivity of sera from patients with RA to A-V and A-VI. Methods: Sera from 26 patients with RA were assessed for anti-A-V and anti-A-VI antibodies and compared with sera from 26 sex/age matched healthy subjects. IgG and IgM antibodies were analyzed in an ELISA. A correlation study with disease activity and corticosteroid treatment schedule was performed. Results: Sera from patients with RA contained significantly higher levels of IgG (anti-A-V and anti-A-VI) autoantibodies than control sera, both being correlated. This rise in antiannexin antibody titers was correlated with the RA activity score, and negatively correlated with the daily dose of corticosteroids. Conclusion: High levels of IgG (anti-A-V and anti-A-VI) antibodies were found in sera from patients with RA. We suggest that antiannexin autoantibodies may play a role in the clinical course of RA by impairing the anti-PLA-2 effect of **annexins**.

L7 ANSWER 23 OF 53 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
AN 1995:108765 BIOSIS
DN PREV199598123065
TI Prevalence and Characteristics of Anti-56K/Annexin XI Autoantibodies in Systemic Autoimmune Diseases.
AU Misaki, Yoshikata; Van Venrooij, Walther J.; Pruijn, Ger J. M. [Reprint author]
CS Dep. Biochem., Univ. Nijmegen, P.O. Box 9101, NL-6500 HB Nijmegen, Netherlands
SO Journal of Rheumatology, (1995) Vol. 22, No. 1, pp. 97-102.
CODEN: JRHUA9. ISSN: 0315-162X.
DT Article
LA English
ED Entered STN: 13 Mar 1995
Last Updated on STN: 13 Mar 1995
AB Objective: To investigate the occurrence and features of anti-56K/**annexin** XI autoantibodies in sera from patients with various systemic autoimmune diseases, including rheumatoid **arthritis**, systemic lupus erythematosus, Sjogren's syndrome, systemic sclerosis, polymyositis and Raynaud's phenomenon. Methods. Anti-56K/**annexin** XI autoantibodies were detected by an enzyme linked immunosorbent assay using the bacterially expressed recombinant protein as antigen. Results: Anti-56K/**annexin** XI autoantibodies were found in a substantial number of patient sera (4.1-10.1%), but are rarely detected in sera from healthy controls and from patients with infectious diseases. Disease specificity was not observed. The majority of these autoantibodies belong to the IgG class and their titers in positive sera are at least as high as those of other well defined autoantibodies. Conclusion: Anti-56K/**annexin** XI autoantibodies frequently occur in systemic autoimmune diseases in contrast to infectious diseases and healthy individuals and are primarily of the IgG isotype, consistent with an antigen driven mechanism of autoantibody production.

L7 ANSWER 24 OF 53 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
AN 1995:21425 BIOSIS
DN PREV199598035725
TI Autoantibodies to annexins: A diagnostic marker for cutaneous disorders?.
AU Bastian, Boris C. [Reprint author]; Nuss, Bernadette; Roemisch, Juergen; Kraus, Michael; Broecker, Eva-B.
CS Dep. Dermatol., Univ. Wuerzburg, Josef-Schneider-Str. 2, D-97080 Wuerzburg, Germany
SO Journal of Dermatological Science, (1994) Vol. 8, No. 3, pp. 194-202.
CODEN: JDSCEI. ISSN: 0923-1811.
DT Article
LA English
ED Entered STN: 11 Jan 1995
Last Updated on STN: 11 Jan 1995
AB **Annexins**/lipocortins are a group of structurally related calcium and lipid binding proteins which have been implicated as mediators of the anti-inflammatory action of corticosteroids. Autoantibodies against **annexin**-1 have been reported in association with autoimmune

diseases such as systemic lupus erythematosus and rheumatoid **arthritis** and their presence has been hypothesized as the reason for the steroid resistance phenomenon. In this study we investigated IgG- and IgM-autoantibodies against **annexin**-1,-2,-3,-4,-5 and -6 in sera of 221 patients with skin disorders and 114 healthy blood donors with newly established ELISAs. Patients were clustered into 5 groups according to their diagnosis: autoimmune diseases, psoriasis, leg ulcer, malignant melanoma, and miscellaneous diseases. Autoantibodies directed against each **annexin** were detectable in all investigated groups, in the control group as well as in the disease groups, without displaying any significant correlation to any of the disease states. The homogenous distribution of **annexin**-autoantibodies throughout the control group and all the disease groups studied, do not support the implication of **annexin**-autoantibodies in pathophysiological states and make them an unlikely candidate for use as a diagnostic marker.

L7 ANSWER 25 OF 53 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
AN 1994:177870 BIOSIS
DN PREV199497190870
TI The 56K autoantigen is identical to human annexin XI.
AU Misaki, Yoshikata; Pruijn, Ger J. M.; Van Der Kemp, Annemiete W. C. M.; Van Venrooij, Walther J. [Reprint author]
CS Dep. Biochem., Univ. Nijmegen, P.O. Box 9101, NL-6500 HB Nijmegen, Netherlands
SO Journal of Biological Chemistry, (1994) Vol. 269, No. 6, pp. 4240-4246. CODEN: JBCHA3. ISSN: 0021-9258.
DT Article
LA English
ED Entered STN: 26 Apr 1994
Last Updated on STN: 26 Apr 1994
AB Anti-56K autoantibodies are present in sera from patients with various autoimmune diseases, predominantly in sera from patients with rheumatoid **arthritis**, systemic lupus erythematosus, or Sjogren's syndrome. To clarify the molecular structure of this autoantigen, we isolated a 2.0-kilobase pair cDNA clone considered to encode the full-length 56K autoantigen. The longest open reading frame encodes a 505-amino acid polypeptide, with a predicted molecular mass of 54.4 kDa. The in vitro translated protein is recognized by all anti-56K positive patient sera tested. Antibodies affinity-purified using the bacterially expressed recombinant protein recognized the 56K autoantigen in a HeLa cell extract. cDNA sequencing revealed that the 56K cDNA shares a high degree of homology in both nucleotide (87%) and amino acid sequence (92.5%) with bovine **annexin** XI, indicating that the 56K cDNA encodes the human homologue of **annexin** XI, a member of the Ca-2+-dependent phospholipid binding protein family. Anti-56K autoantibody exhibits both a cytoplasmic and a nuclear staining in immunofluorescence experiments. Patients' sera recognize preferentially the N-terminal region of the protein, which is specific for 56K/**annexin** XI and not shared by other **annexins**, indicating that the autoimmune response to 56K/**annexin** XI in these patients is specific for this **annexin** family member.

L7 ANSWER 26 OF 53 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
AN 1993:83735 BIOSIS
DN PREV199344037985
TI Specific binding of lipocortin-1 (**annexin** I) to monocytes and neutrophils is decreased in rheumatoid **arthritis**.
AU Goulding, Nicolas J. [Reprint author]; Jefferiss, Carolyn M. [Reprint author]; Pan, Luying; Rigby, William F. C.; Guyre, Paul M.
CS Bath Inst. Rheumatic Disease, Bath, UK
SO Arthritis and Rheumatism, (1992) Vol. 35, No. 11, pp. 1395-1397. CODEN: ARHEAW. ISSN: 0004-3591.
DT Article
LA English
ED Entered STN: 1 Feb 1993
Last Updated on STN: 1 Feb 1993

L7 ANSWER 27 OF 53 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
AN 1992:439729 BIOSIS
DN PREV199243072729; BR43:72729
TI LIPOCORTIN WHAT IS IT AND WHAT DOES IT MEAN?.
AU FLOWER R J [Reprint author]
CS DEP BIOCHEM PHARMACOL, MED COLL ST BARTHOLOMEW'S HOSP, UNIV LONDON, CHARTERHOUSE SQUARE, LONDON EC1M 6BQ, UK
SO British Journal of Rheumatology, (1992) Vol. 31, No. 8, pp. 506-507. ISSN: 0263-7103.
DT Article
FS BR
LA ENGLISH
ED Entered STN: 30 Sep 1992
Last Updated on STN: 30 Sep 1992

L7 ANSWER 28 OF 53 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
AN 2000174050 EMBASE
TI Inhibitory effect of **annexin** I on synovial inflammation in rat adjuvant **arthritis**.
AU Yang Y.; Hutchinson P.; Morand E.F.
CS Dr. E.F. Morand, Centre for Inflammatory Diseases, Monash Univ. Department of Medicine, Monash Medical Centre, Melbourne, Vic. 3168, Australia
SO Arthritis and Rheumatism, (1999) Vol. 42, No. 7, pp. 1538-1544.
Refs: 48
ISSN: 0004-3591 CODEN: ARHEAW
CY United States
DT Journal; Article
FS 030 Pharmacology
031 Arthritis and Rheumatism
037 Drug Literature Index
LA English
SL English
ED Entered STN: 20000531
Last Updated on STN: 20000531
AB Objective. **Annexin** I is an endogenous antiinflammatory mediator, expressed in rheumatoid **arthritis** (RA) synovium, the contribution of which to autoregulation of the synovial inflammatory response has not been examined in models of RA. We investigated the antiinflammatory role of **annexin** I in rat adjuvant **arthritis**. Methods. Rats with adjuvant-induced **arthritis** (AIA) were treated with a specific anti-**annexin** I monoclonal antibody (mAb), isotype control IgG, and/or dexamethasone. Clinical outcomes and synovial synthesis of tumor necrosis factor α (TNFα), prostaglandin E2 (PGE2), and nitric oxide were examined, and **annexin** I expression was assessed by flow cytometry and reverse transcription-polymerase chain reaction. Results. Anti-**annexin** I mAb reversed the effects of dexamethasone on the clinical features of AIA and exacerbated AIA in the absence of exogenous glucocorticoid. Clinical exacerbation of AIA by anti-**annexin** I mAb was accompanied by significantly increased synovial TNFα and PGE2, suggesting that **annexin** I tonically inhibits the production of these mediators. Anti-**annexin** I mAb treatment was associated with significantly reduced leukocyte intracellular **annexin** I, despite increased **annexin** I messenger RNA expression, consistent with a depletion effect of extracellular mAb via the cell surface. Conclusion. **Annexin** I is a key endogenous inhibitory mediator of **arthritis** via mechanisms that include inhibition of cytokine and effector molecule production. Moreover, a synthesis-independent depletion of intracellular **annexin** I by extracellular antibody supports the hypothesis that externalization of **annexin** I is involved in its mode of action.

L7 ANSWER 29 OF 53 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
AN 1999335818 EMBASE

TI Lymphocyte apoptosis in systemic lupus erythematosus: Relationships with Fas expression, serum soluble Fas and disease activity.
AU Courtney P.A.; Crockard A.D.; Williamson K.; McConnell J.; Kennedy R.J.; Bell A.L.
CS P.A. Courtney, Department Rheumatology Immunology, Musgrove Park Hospital, Stockman's Lane, Belfast BT0 7JB, United Kingdom
SO Lupus, (1999) Vol. 8, No. 7, pp. 508-513.
Refs: 32
ISSN: 0961-2033 CODEN: LUPUES
CY United Kingdom
DT Journal; Article
FS 005 General Pathology and Pathological Anatomy
026 Immunology, Serology and Transplantation
031 Arthritis and Rheumatism
LA English
SL English
ED Entered STN: 19991017
Last Updated on STN: 19991017
AB Lupus specific autoantigens are exposed on apoptotic cells. The increased number of apoptotic lymphocytes reported in systemic lupus erythematosus (SLE) may be attributable to abnormalities of lymphocyte Fas expression or serum soluble Fas. In the present study we analysed the count of circulating apoptotic lymphocytes in SLE patients (n = 50), by flow cytometry using **Annexin** V, compared to rheumatoid **arthritis** patients (RA, n = 20), inflammatory bowel disease patients (IBD, n = 20) and normal controls (n = 20). Lymphocyte Fas expression and serum soluble Fas were measured and related to numbers of apoptotic lymphocytes. The percentage of apoptotic lymphocytes, determined by **Annexin** V binding, was significantly increased in peripheral blood of SLE patients (median = 4.2%) compared with normal healthy donors (median = 1.1%) and IBD patients (median = 2.0%) but not RA (median = 3.9%). SLE lymphocyte Fas expression was not significantly different from RA or IBD patients. Serum soluble Fas in SLE patients correlated positively with apoptotic lymphocytes and antibodies to double stranded DNA. This study suggests that increased apoptotic lymphocytes and increased lymphocyte Fas expression may not be specific to SLE. Serum soluble Fas may have a role in the regulation of lymphocyte apoptosis in SLE.

L7 ANSWER 30 OF 53 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
AN 1999175827 EMBASE
TI Increased apoptotic peripheral blood neutrophils in systemic lupus erythematosus: Relations with disease activity, antibodies to double stranded DNA, and neutropenia.
AU Courtney P.A.; Crockard A.D.; Williamson K.; Irvine A.E.; Kennedy R.J.; Bell A.L.
CS Dr. P.A. Courtney, Department of Rheumatology, Musgrave Park Hospital, Stockman's Lane, Belfast BT9 7JB, United Kingdom
SO Annals of the Rheumatic Diseases, (1999) Vol. 58, No. 5, pp. 309-314.
Refs: 44
ISSN: 0003-4967 CODEN: ARDIAO
CY United Kingdom
DT Journal; Article
FS 026 Immunology, Serology and Transplantation
031 Arthritis and Rheumatism
LA English
SL English
ED Entered STN: 19990610
Last Updated on STN: 19990610
AB Objective - To quantify the percentage of apoptotic peripheral blood neutrophils in systemic lupus erythematosus (SLE) and to determine the relations with disease activity and neutropenia. Methods - Neutrophil apoptosis in SLE patients (n = 50) was assessed by flow cytometry using **annexin** V binding and fluorescent labelled anti-fas. Rheumatoid **arthritis** (RA, n = 20) and inflammatory bowel disease patients (IBD, n = 20) were studied as disease controls. Results - The percentage of apoptotic neutrophils, determined by **annexin** V binding, was

increased in peripheral blood of SLE patients (median = 3.25%) compared with normal healthy donors (n =20, median = 1.20%) and disease controls (RA: median = 1.15%) (IBD: median = 1.15%). SLE neutrophil apoptosis correlated positively with lupus disease activity measured by SLAM score. SLE patients with increased antibodies to dsDNA (>10 mg/ml) had increased apoptotic neutrophils. Eight of 14 neutropenic SLE patients had increased apoptotic neutrophils. Increased neutrophil fas expression compared with normal controls was observed in SLE, RA, and IBD. Conclusion - Neutrophil fas expression is increased non- specifically in inflammatory disease. Increased circulating apoptotic neutrophils in SLE correlate positively with disease activity (SLAM) and may contribute to autoantigen excess including dsDNA.

L7 ANSWER 31 OF 53 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
AN 1998364607 EMBASE
TI Novel pathways for glucocorticoid effects on neutrophils in chronic inflammation.
AU Goulding N.J.; Euzger H.S.; Butt S.K.; Perretti M.
CS N.J. Goulding, Arthritis Research Section, St. Bartholomew's and Royal London, School of Medicine and Dentistry, Charterhouse Square, London EC1M 6BQ, United Kingdom
SO Inflammation Research, (1998) Vol. 47, No. SUPPL. 3, pp. S158-S165.
Refs: 68
ISSN: 1023-3830 CODEN: INREFB
CY Switzerland
DT Journal; Conference Article
FS 030 Pharmacology
031 Arthritis and Rheumatism
037 Drug Literature Index
LA English
SL English
ED Entered STN: 19981119
Last Updated on STN: 19981119
AB Neutrophils have been implicated in mediating much of the tissue damage associated with chronic inflammatory diseases such as rheumatoid **arthritis**, where they are involved in destruction of both cartilage and bone. Glucocorticoids are powerful anti-inflammatory agents, often used in the treatment of this autoimmune disease. They exert significant inhibitory effects on neutrophil activation and functions, such as chemotaxis, adhesion, transmigration, apoptosis, oxidative burst, and phagocytosis. The mechanisms by which glucocorticoids exert these effects on neutrophils are unclear. Evidence from studies of inflammation in human subjects and animal models suggests that **annexin**-I, an endogenous, glucocorticoid-induced protein also known as lipocortin-1, has a pivotal role in modulating neutrophil activation, transmigratory, and phagocytic functions. Furthermore, we present evidence for altered neutrophil functions in rheumatoid **arthritis** that correspond to a significantly reduced capacity of these cells to bind **annexin**-I. A proposed novel pathway for glucocorticoid actions on neutrophils involving **annexin**-I could explain the development of chronic neutrophil activation in diseases such as rheumatoid **arthritis**.

L7 ANSWER 32 OF 53 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
AN 1998075588 EMBASE
TI Synovial fibroblasts and the sphingomyelinase pathway: Sphingomyelin turnover and ceramide generation are not signaling mechanisms for the actions of tumor necrosis factor-α.
AU Gerritsen M.E.; Shen C.-P.; Perry C.A.
CS Dr. M.E. Gerritsen, Genentech, One DNA Way, South San Francisco, CA 94080, United States. meg@gene.com
SO American Journal of Pathology, (1998) Vol. 152, No. 2, pp. 505-512.
Refs: 28
ISSN: 0002-9440 CODEN: AJPAA4
CY United States
DT Journal; Article

FS 005 General Pathology and Pathological Anatomy
LA English
SL English
ED Entered STN: 19980409
Last Updated on STN: 19980409
AB The activation of sphingomyelinase and the generation of ceramide has been proposed to mediate tumor necrosis factor-α (TNF-α)-induced nuclear factor (NF)-κB activation through its second messenger ceramide. Ceramide may also be an important regulator of cell growth, senescence, and apoptosis. Aberrant cell proliferation and apoptosis have been implicated in the rampant fibroblast proliferation and pannus formation characteristic of rheumatoid **arthritis**. However, the role of TNF-α and the sphingomyelinase pathway in the process have not been determined. The objective of this study was to determine whether TNF-α activates the sphingomyelin pathway in human synovial fibroblasts (HSF) and the potential role of ceramide in HSF proliferation and apoptosis. Cultured human synovial fibroblasts were stimulated with exogenous TNF-α, sphingomyelinase, and ceramide. Apoptosis was assessed by cell morphology and **annexin** V labeling. NF-κB and stress kinase pathway activation were determined by immunoblotting techniques. Sphingomyelinase activation was determined by quantitation of sphingomyelin and ceramide radioactivity in [14C]serine-prelabeled HSF cells. The addition of TNF-α (50 ng/ml) to HSF did not elicit detectable sphingomyelinase activation. TNF-α was shown to activate NF-κB (p65 translocation and degradation of Iκβα) and the stress kinase pathway (phosphorylation of ATF-2, p38, and c-jun). In contrast, exogenous ceramide had no effect on these signaling pathways nor did ceramide stimulate the generation of interleukin-6 or interleukin-8. High concentrations of ceramide (≤25 μmol/L) were cytotoxic, whereas lower concentrations of ceramide inhibited cell cycle progression. Thus, although TNF-α stimulates the NF- κB and stress kinase pathways in HSF, these effects of TNF-α are not associated with sphingomyelinase turnover or induction of apoptosis.

L7 ANSWER 33 OF 53 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
AN 97268752 EMBASE
DN 1997268752
TI Annexins in cancer and autoimmune diseases.
AU Bastian B.C.
CS B.C. Bastian, Cancer Genetics Program, University California San Francisco, Cancer Center, Box 0808, San Francisco, CA 94143-0808, United States. bastian@cc.ucsf.edu
SO Cellular and Molecular Life Sciences, (1997) Vol. 53, No. 6, pp. 554-556.
Refs: 44
ISSN: 1420-682X CODEN: CMLSFI
CY Switzerland
DT Journal; Article
FS 005 General Pathology and Pathological Anatomy
026 Immunology, Serology and Transplantation
029 Clinical Biochemistry
LA English
SL English
ED Entered STN: 970925
Last Updated on STN: 970925
AB Several **annexins** have been implicated in the pathogenesis of benign and malignant neoplasms of different origins. In some tumours a suppressive action of **annexins** has been shown, whereas studies of other tumours indicate an involvement of **annexins** in tumour progression. In the light of the expression of **annexins** at distinct episodes of fetal development these observations point towards a functional role of **annexins** in cellular development and differentiation. This view is supported by data that link certain **annexins** to distinct pathways of signal transduction.
Auto-antibodies against several **annexins** have been detected in patients with autoimmune diseases such as systemic lupus erythematosus, rheumatoid **arthritis** and inflammatory bowel disease. Until now it is unclear whether their presence reflects a relevant pathogenetic

mechanism or merely represents an unspecific expression of a raised autoimmunity in these patients.

L7 ANSWER 34 OF 53 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
AN 97003932 EMBASE
DN 1997003932
TI **Annexin** V autoantibodies in rheumatoid **arthritis**.
AU Rodriguez-Garcia M.I.; Fernandez J.A.; Rodriguez A.; Fernandez M.P.; Gutierrez C.; Torre-Alonso J.C.
CS J.C. Torre-Alonso, Dept. Biochemistry/Molecular Biology, University of Oviedo, Faculty of Medicine, E-33006 Oviedo, Spain
SO Annals of the Rheumatic Diseases, (1996) Vol. 55, No. 12, pp. 895-900. Refs: 32
ISSN: 0003-4967 CODEN: ARDIAO
CY United Kingdom
DT Journal; Article
FS 020 Gerontology and Geriatrics
026 Immunology, Serology and Transplantation
031 Arthritis and Rheumatism
037 Drug Literature Index
LA English
SL English
ED Entered STN: 970212
Last Updated on STN: 970212
AB Objective - To investigate the occurrence of anti-annerbn V autoantibodies in sera of patients with rheumatoid **arthritis** to assess involvement with the disease and any relation to glucocorticoid treatment. Methods - Anti-annerrin V antibodies were measured by an enzyme linked immunesorbent assay (ELISA) which used the purified human recombinant protein as antigen. Results - Concentrations of anti-annerrin V autoantibodies, predominantly of the IgG class, were significantly raised in sera from patients with rheumatoid **arthritis** compared to normal controls. This was not correlated with other indices of disease activity such as erythrocyte sedimentation rate or C reactive protein and was unrelated to glucocorticoid treatment. Conclusions-Extracellular **annexin** V provides an antigenic stimulus for autoantibody production and its in vivo expression is independent of glucocorticoid control. Such autoantibodies may have a detrimental role in the **arthritic** condition by interfering with putative functions of **annexin** V, including collagen type II binding, inhibition of phospholipase A2 activity, and Fc receptor activity.

L7 ANSWER 35 OF 53 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
AN 95306913 EMBASE
DN 1995306913
TI Differential distribution of annexins-I, -II, -IV, and -VI in synovium.
AU Goulding N.J.; Dixey J.; Morand E.F.; Dodds R.A.; Wilkinson L.S.; Pitsillides A.A.; Edwards J.C.W.
CS Department of Rheumatology, Medical College, St Bartholomew's Hospital, Charterhouse Square,London EC1M 6BQ, United Kingdom
SO Annals of the Rheumatic Diseases, (1995) Vol. 54, No. 10, pp. 841-845.
ISSN: 0003-4967 CODEN: ARDIAO
CY United Kingdom
DT Journal; Article
FS 005 General Pathology and Pathological Anatomy
031 Arthritis and Rheumatism
LA English
SL English
ED Entered STN: 951114
Last Updated on STN: 951114
AB Objectives - To examine the distribution of four **annexins** in non-inflamed rheumatoid **arthritic** and osteoarthritic synovial tissue. Methods - Frozen sections were stained with monoclonal antibodies (MAb) specific for **annexins**-I -II, -IV, and -VI, and for cell lineage related markers including CD68 and CD14 (macrophages), prolyl hydroxylase (fibroblasts), and CD3 (T cells). Results - Each of the

annexins was present in synovial tissues in significant amounts in the three groups studied. **Annexin**-I was predominantly found within the synovial lining layer and double labelling showed it to be present predominantly in cells of the macrophage lineage. In rheumatoid specimens there was increased staining within the lining layer, perivascularly and on macrophages within the tissue stroma. **Annexin**-II was present in a distribution similar to that of **annexin**-I, but with more prominent perivascular staining. **Annexins**-IV and -VI were seen chiefly in association with areas of lymphocyte infiltration in rheumatoid tissue, whereas **annexins**-I and -II were absent from these areas. Endothelial cells stained weakly positive for **annexins**-I and -II, and more strongly for -IV and -VI. Conclusions - This study demonstrates that **annexins** (particularly **annexin**-I, a putative mediator of the anti-inflammatory activities of glucocorticoids) are abundant in rheumatoid and nonrheumatoid synovial tissue, **annexins** -IV and -VI having a distribution distinct from that of -I and -II.

L7 ANSWER 36 OF 53 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
AN 95199727 EMBASE
DN 1995199727
TI High levels of antibodies to **annexins** V and VI in patients with rheumatoid **arthritis**.
AU Dubois T.; Bisagni-Faure A.; Coste J.; Mavoungou E.; Menkes C.-J.; Russo-Marie F.; Rothhut B.
CS INSERM U. 332, ICGM, 22 Rue Mechain,75014 Paris, France
SO Journal of Rheumatology, (1995) Vol. 22, No. 7, pp. 1230-1234. ISSN: 0315-162X CODEN: JRHUA
CY Canada
DT Journal; Article
FS 026 Immunology, Serology and Transplantation
031 Arthritis and Rheumatism
037 Drug Literature Index
LA English
SL English
ED Entered STN: 950809
Last Updated on STN: 950809
AB Objective. Glucocorticoids are powerful antiinflammatory agents widely used for the treatment of rheumatoid **arthritis** (RA). Synthesis and/or secretion of **annexin** I (A-I) is induced by these steroids. **Annexins** V and VI are also found extracellularly but are not induced by glucocorticoids. **Annexins** may be potent antagonists of phospholipase A2 (PLA2). Since autoantibodies to A-I have been reported in patients with RA, we studied the reactivity of sera from patients with RA to A-V and A-VI. Methods. Sera from 26 patients with RA were assessed for anti-A-V and anti-A-VI antibodies and compared with sera from 26 sex/age matched healthy subjects. IgG and IgM antibodies were analyzed in an ELISA. A correlation study with disease activity and corticosteroid treatment schedule was performed. Results. Sera from patients with RA contained significantly higher levels of IgG [anti-A-V and anti-A-VI] autoantibodies than control sera, both being correlated. This rise in antiannexin antibody titers was correlated with the RA activity score, and negatively correlated with the daily dose of corticosteroids. Conclusion. High levels of IgG (anti-A-V and anti-A-VI) antibodies were found in sera from patients with RA. We suggest that antiannexin autoantibodies may play a role in the clinical course of RA by impairing the anti-PLA2 effect of **annexins**.

L7 ANSWER 37 OF 53 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
AN 95022817 EMBASE
DN 1995022817
TI Prevalence and characteristics of anti-56K/annexin XI autoantibodies in systemic autoimmune diseases.
AU Misaki Y.; Van Venrooij W.J.; Pruijn G.J.M.
CS Department of Biochemistry, University of Nijmegen, PO Box 9101,NL-6500 HB Nijmegen, Netherlands

SO Journal of Rheumatology, (1995) Vol. 22, No. 1, pp. 97-102.
ISSN: 0315-162X CODEN: JRHUA
CY Canada
DT Journal; Article
FS 006 Internal Medicine
011 Otorhinolaryngology
013 Dermatology and Venereology
026 Immunology, Serology and Transplantation
031 Arthritis and Rheumatism
LA English
SL English
ED Entered STN: 950215
Last Updated on STN: 950215
AB Objective. To investigate the occurrence and features of anti-56K/**annexin** XI autoantibodies in sera from patients with various systemic autoimmune diseases, including rheumatoid **arthritis**, systemic lupus erythematosus, Sjogren's syndrome, systemic sclerosis, polymyositis and Raynaud's phenomenon. Methods. Anti-56K-**annexin** XI autoantibodies were detected by an enzyme linked immunosorbent assay using the bacterially expressed recombinant protein as antigen. Results. Anti-56K/**annexin** XI autoantibodies were found in a substantial number of patient sera (4.1-10.1%), but are rarely detected in sera from healthy controls and from patients with infectious diseases. Disease specificity was not observed. The majority of these autoantibodies belong to the IgG class and their titers in positive sera are at least as high as those of other well defined autoantibodies. Conclusion. Anti-56K-**annexin** XI autoantibodies frequently occur in systemic autoimmune diseases in contrast to infectious diseases and healthy individuals and are primarily of the IgG isotype, consistent with an antigen driven mechanism of autoantibody production.

L7 ANSWER 38 OF 53 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
AN 94352825 EMBASE
DN 1994352825
TI Autoantibodies to annexins: A diagnostic marker for cutaneous disorders?.
AU Bastian B.C.; Nuss B.; Romisch J.; Kraus M.; Brocker E.
CS Department of Dermatology, University of Wurzburg, Josef-Schneider-Str. 2,D-97080 Wurzburg, Germany
SO Journal of Dermatological Science, (1994) Vol. 8, No. 3, pp. 194-202.
ISSN: 0923-1811 CODEN: JDSCEI
CY Ireland
DT Journal; Article
FS 013 Dermatology and Venereology
029 Clinical Biochemistry
LA English
SL English
ED Entered STN: 941221
Last Updated on STN: 941221
AB **Annexins**/lipocortins are a group of structurally related calcium and lipid binding proteins which have been implicated as mediators of the anti-inflammatory action of corticosteroids. Autoantibodies against **annexin**-1 have been reported in association with autoimmune diseases such as systemic lupus erythematosus and rheumatoid **arthritis** and their presence has been hypothesized as the reason for the steroid resistance phenomenon. In this study we investigated IgG- and IgM-autoantibodies against **annexin**-1,-2,-3,-4,-5 and -6 in sera of 221 patients with skin disorders and 114 healthy blood donors with newly established ELISAs. Patients were clustered into 5 groups according to their diagnosis: autoimmune diseases, psoriasis, leg ulcer, malignant melanoma, and miscellaneous diseases. Autoantibodies directed against each **annexin** were detectable in all investigated groups, in the control group as well as in the disease groups, without displaying any significant correlation to any of the disease states. The homogenous distribution of **annexin**-autoantibodies throughout the control group and all the disease groups studied, do not support the implication of **annexin**-autoantibodies in pathophysiological states and make them an unlikely candidate for use as a diagnostic marker.

L7 ANSWER 39 OF 53 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
AN 94238647 EMBASE
DN 1994238647
TI The 56K autoantigen is identical to human annexin XI.
AU Misaki Y.; Pruijn G.J.M.; Van der Kemp A.W.C.M.; Van Venrooij W.J.
CS Dept. of Biochemistry, University of Nijmegen, P. O. Box 9101,NL-6500 HB Nijmegen, Netherlands
SO Journal of Biological Chemistry, (1994) Vol. 269, No. 6, pp. 4240-4246. ISSN: 0021-9258 CODEN: JBCHA3
CY United States
DT Journal; Article
FS 026 Immunology, Serology and Transplantation
029 Clinical Biochemistry
LA English
SL English
ED Entered STN: 940826
Last Updated on STN: 940826
AB Anti-56K autoantibodies are present in sera from patients with various autoimmune diseases, predominantly in sera from patients with rheumatoid **arthritis**, systemic lupus erythematosus, or Sjogren's syndrome. To clarify the molecular structure of this autoantigen, we isolated a 2.0-kilobase pair cDNA clone considered to encode the full-length 56K autoantigen. The longest open reading frame encodes a 505-amino acid polypeptide, with a predicted molecular mass of 54.4 kDa. The in vitro translated protein is recognized by all anti-56K positive patient sera tested. Antibodies affinity-purified using the bacterially expressed recombinant protein recognized the 56K autoantigen in a HeLa cell extract. cDNA sequencing revealed that the 56K cDNA shares a high degree of homology in both nucleotide (87%) and amino acid sequence (92.5%) with bovine **annexin** XI, indicating that the 56K cDNA encodes the human homologue of **annexin** XI, a member of the Ca2+-dependent phospholipid binding protein family. Anti-56K autoantibody exhibits both a cytoplasmic and a nuclear staining in immunofluorescence experiments. Patients' sera recognize preferentially the N-terminal region of the protein, which is specific for 56K/**annexin** XI and not shared by other **annexins**, indicating that the autoimmune response to 56K/**annexin** XI in these patients is specific for this **annexin** family member.

L7 ANSWER 40 OF 53 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
AN 92342074 EMBASE
DN 1992342074
TI Specific binding of lipocortin-1 (**annexin** I) to monocytes and neutrophils is decreased in rheumatoid **arthritis**.
AU Goulding N.J.; Jefferiss C.M.; Pan L.; Rigby W.F.C.; Guyre P.M.
CS Bath Inst. for Rheumatic Diseases,Bath, United Kingdom
SO Arthritis and Rheumatism, (1992) Vol. 35, No. 11, pp. 1395-1397. ISSN: 0004-3591 CODEN: ARHEAW
CY United States
DT Journal; Article
FS 026 Immunology, Serology and Transplantation
029 Clinical Biochemistry
031 Arthritis and Rheumatism
LA English
ED Entered STN: 921213
Last Updated on STN: 921213
DATA NOT AVAILABLE FOR THIS ACCESSION NUMBER

L7 ANSWER 41 OF 53 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 1999:476258 HCAPLUS
DN 132:22041
TI Inhibitory effect of **annexin** I on synovial inflammation in rat adjuvant **arthritis**
AU Yang, Yuanhang; Hutchinson, Paul; Morand, Eric F.
CS Monash University, Melbourne, 3168, Australia

SO Arthritis & Rheumatism (**1999**), 42(7), 1538-1544
CODEN: ARHEAW; ISSN: 0004-3591
PB Lippincott Williams & Wilkins
DT Journal
LA English
AB **Annexin** I is an endogenous antiinflammatory mediator, expressed in rheumatoid **arthritis** (RA) synovium, the contribution of which to autoregulation of the synovial inflammatory response has not been examined in models of RA. We investigated the anti-inflammatory role of **annexin** I in rat adjuvant **arthritis**. Rats with adjuvant-induced **arthritis** (AIA) were treated with a specific anti-**annexin** I monoclonal antibody (mAb), isotype control IgG, and/or dexamethasone. Clin. outcomes and synovial synthesis of tumor necrosis factor α (TNFα), prostaglandin E2 (PGE2), and nitric oxide were examined, and **annexin** I expression was assessed by flow cytometry and reverse transcription-polymerase chain reaction. Anti-**annexin** I mAb reversed the effects of dexamethasone on the clin. features of AIA and exacerbated AIA in the absence of exogenous glucocorticoid. Clin. exacerbation of AIA by anti-**annexin** I mAb was accompanied by significantly increased synovial TNFα and PGE2, suggesting that **annexin** I tonically inhibits the production of these mediators. Anti-**annexin** I mAb treatment was associated with significantly reduced leukocyte intracellular **annexin** I, despite increased **annexin** I mRNA expression, consistent with a depletion effect of extracellular mAb via the cell surface. **Annexin** I is a key endogenous inhibitory mediator of **arthritis** via mechanisms that include inhibition of cytokine and effector mol. production Moreover, a synthesis-independent depletion of intracellular **annexin** I by extracellular antibody supports the hypothesis that externalization of **annexin** I is involved in its mode of action.
RE.CNT 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 42 OF 53 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 1998:709458 HCAPLUS
DN 129:298527
TI Novel pathways for glucocorticoid effects on neutrophils in chronic inflammation
AU Goulding, N. J.; Euzger, H. S.; Butt, S. K.; Perretti, M.
CS Arthritis Research Section, St. Bartholomew's Royal London School Medicine Dentistry, London, EC1M 6BQ, UK
SO Inflammation Research (**1998**), 47(Suppl.3), S158-S165
CODEN: INREFB; ISSN: 1023-3830
PB Birkhaeuser Verlag
DT Journal; General Review
LA English
AB Neutrophils were implicated in mediating much of the tissue damage associated with chronic inflammatory diseases such as rheumatoid **arthritis**, where they are involved in destruction of both cartilage and bone. Glucocorticoids are powerful anti-inflammatory agents, often used in the treatment of this autoimmune disease. They exert significant inhibitory effects on neutrophil activation and functions, such as chemotaxis, adhesion, transmigration, apoptosis, oxidative burst, and phagocytosis. The mechanisms by which glucocorticoids exert these effects on neutrophils are unclear. Evidence from studies of inflammation in human subjects and animal models suggests that **annexin**-I, an endogenous, glucocorticoid-induced protein also known as lipocortin-1, has a pivotal role in modulating neutrophil activation, transmigratory, and phagocytic functions. The authors present evidence for altered neutrophil functions in rheumatoid **arthritis** that correspond to a reduced capacity of these cells to bind **annexin**-I. A proposed novel pathway for glucocorticoid actions on neutrophils involving **annexin**-1 could explain the development of chronic neutrophil activation in diseases such as rheumatoid **arthritis**. A review is added.

L7 ANSWER 43 OF 53 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 1998:121036 HCAPLUS
DN 128:191560

TI Synovial fibroblasts and the sphingomyelinase pathway: sphingomyelin turnover and ceramide generation are not signaling mechanisms for the actions of tumor necrosis factor-α
AU Gerritsen, Mary E.; Shen, Chien-Ping; Perry, Carol A.
CS Institute for Bone and Joint Disease and Cancer, Bayer Corporation, West Haven, CT, USA
SO American Journal of Pathology (**1998**), 152(2), 505-512
CODEN: AJPAA4; ISSN: 0002-9440
PB American Society for Investigative Pathology
DT Journal
LA English
AB The activation of sphingomyelinase and the generation of ceramide has been proposed to mediate tumor necrosis factor-α (TNF-α)-induced nuclear factor (NF)-κB activation through its second messenger ceramide. Ceramide may also be an important regulator of cell growth, senescence, and apoptosis. Aberrant cell proliferation and apoptosis have been implicated in the rampant fibroblast proliferation and pannus formation characteristic of rheumatoid **arthritis**. However, the role of TNF-α and the sphingomyelinase pathway in the process have not been determined The objective here was to determine whether TNF-α activates the sphingomyelin pathway in human synovial fibroblasts (HSF) and the potential role of ceramide in HSF proliferation and apoptosis. Cultured human synovial fibroblasts were stimulated with exogenous TNF-α, sphingomyelinase, and ceramide. Apoptosis was assessed by cell morphol. and **annexin** V labeling. NF-κB and stress kinase pathway activation were determined by immunoblotting techniques. Sphingomyelinase activation was determined by quantitation of sphingomyelin and ceramide radioactivity in [14C]serine-prelabeled HSF cells. The addition of TNF-α (50 ng/mL) to HSF did not elicit detectable sphingomyelinase activation. TNF-α was shown to activate NF-κB (p65 translocation and degradation of IκBα) and the stress kinase pathway (phosphorylation of ATF-2, p38, and c-jun). In contrast, exogenous ceramide had no effect on these signaling pathways nor did ceramide stimulate the generation of interleukin-6 or interleukin-8. High concns. of ceramide (≥25 μmol/L) were cytotoxic, whereas lower concns. of ceramide inhibited cell cycle progression. Thus, although TNF-α stimulates the NF-κB and stress kinase pathways in HSF, these effects of TNF-α are not associated with sphingomyelinase turnover or induction of apoptosis.
RE.CNT 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 44 OF 53 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 1998:97306 HCAPLUS
DN 128:201145
TI Glucocorticoid inhibition of adjuvant arthritis synovial macrophage nitric oxide production: role of lipocortin 1
AU Yang, Y. H.; Hutchinson, P.; Santos, L. L.; Morand, E. F.
CS University Department of Medicine, Centre for Inflammatory Diseases, Monash Medical Centre, Clayton, 3168, Australia
SO Clinical and Experimental Immunology (**1998**), 111(1), 117-122
CODEN: CEXIAL; ISSN: 0009-9104
PB Blackwell Science Ltd.
DT Journal
LA English
AB Nitric oxide (NO) is a mediator of inflammatory injury which is inhibited by glucocorticoids and is implicated in rheumatoid (RA) and adjuvant arthritis (AA). The glucocorticoid-induced anti-inflammatory mol. lipocortin 1 is expressed in RA synovium, but the effects of lipocortin 1 on synovial inflammation have been little studied. The authors investigated the effects of glucocorticoids and lipocortin 1 on inducible NO synthase (iNOS) and glucocorticoids on the induction of lipocortin 1 in AA synovial macrophages. NO production was measured by Griess assay in supernatants of day 14 AA rat synovial explants and of synovial macrophages purified from enzyme-digested synovium and treated with lipopolysaccharide (LPS) 1 μg/mL, dexamethasone (DEX) 10-7 M, and anti-lipocortin 1 MoAb. The iNOS and lipocortin 1 expression were detected by flow cytometry using specific MoAb. Cell surface lipocortin

was determined by Western blot. NO was produced by all AA synovial explants and NO was released by cultured synovial macrophages (14.5 μmol/24 h). The iNOS was detected in synovial macrophages (ED-1+) by permeabilization flow cytometry. LPS increased synovial macrophage NO release and iNOS expression. DEX inhibited constitutive and LPS-induced NO release and iNOS expression. DEX inhibition of synovial macrophage NO was associated with induction of cell surface and intracellular lipocortin 1. Anti-lipocortin 1 MoAb treatment reduced the inhibition of NO release by DEX, but had no effect on iNOS expression. These findings demonstrate a role for lipocortin 1 in the inhibition by glucocorticoids of AA synovial macrophage iNOS activity.

RE.CNT 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 45 OF 53 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 1998:25043 HCAPLUS
DN 128:97818
TI Antiinflammatory effect of lipocortin 1 in experimental arthritis
AU Yang, Yuanhang; Leech, Michelle; Hutchinson, Paul; Holdsworth, Stephen R.; Morand, Eric F.
CS Monash University Department of Medicine, Monash Medical Centre, Centre for Inflammatory Diseases, Melbourne, Australia
SO Inflammation (New York) (**1997**), 21(6), 583-596
CODEN: INFLD4; ISSN: 0360-3997
PB Plenum Publishing Corp.
DT Journal
LA English
AB The glucocorticoid-induced antiinflammatory protein lipocortin 1 is present in arthritic synovium but its ability to regulate joint inflammation has not previously been studied. The authors investigated the role of lipocortin 1 in the antiinflammatory activity of glucocorticoids in an acute arthritis model induced by intraarticular injection of carrageenan. Compared to control joints (0.09.+-.0.08+106 synovial fluid cell count), carrageenan injected joints exhibited marked infiltration of PMN (10.2±0.7+106, $p < 0.001$). Both i.p. (1.0 mg/kg) and intra-articular administration (5 μg) of dexamethasone (DEX) significantly suppressed arthritis severity ($p < 0.001$ and 0.005, resp.), and the effects of DEX were significantly prevented by intra-articular injection of antilipocortin 1 mAb ($p < 0.05$). Carrageenan arthritis was also significantly inhibited by intraarticular administration of the N-terminal lipocortin 1 peptide Ac2-26 at doses of 1 or 2 mg/kg ($p < 0.01$). Intra-articular injection antilipocortin 1 mAb in the absence of DEX also significantly exacerbated arthritis severity ($p < 0.005$). In vitro treatment of PMN with DEX was associated with significant inhibition of phagocytosis ($p < 0.005$) and reactive oxygen species (ROS) generation ($p < 0.001$). Antilipocortin 1 mAb significantly reduced the inhibitory effects of DEX ($p < 0.01$ and 0.005, resp.). These results demonstrate that lipocortin 1 mediates the effects of exogenous glucocorticoids on neutrophil migration in carrageenan-induced acute arthritis, exerts an endogenous antiinflammatory influence, and mediates glucocorticoid inhibition of neutrophil activation.

RE.CNT 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 46 OF 53 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 1997:674652 HCAPLUS
DN 127:345208
TI Molecular determinants of monosodium urate crystal-induced murine peritonitis: a role for endogenous mast cells and a distinct requirement for endothelial-derived selectins
AU Getting, Stephen J.; Flower, Roderick J.; Parente, Luca; De Medicis, Rinaldo; Lussier, Andre; Woliztky, Barry A.; Martins, Marco A.; Perretti, Mauro
CS Department of Biochemical Pharmacology, The William Harvey Research Institute, London, UK
SO Journal of Pharmacology and Experimental Therapeutics (**1997**), 283(1), 123-130
CODEN: JPETAB; ISSN: 0022-3565

PB Williams & Wilkins
DT Journal
LA English
AB Injection of monosodium urate (MSU) crystals, the etiol. cause of gouty arthritis, into murine peritoneal cavities produced an intense recruitment of polymorphonuclear leukocytes (PMN). After 3 mg MSU crystal injection, cell influx was maximal (.apprx. 10+106 cells per mouse) at 6 h postinjection and sustained up to the 24 h time-point. In mice depleted of mast cells by administration of compound 48/80 72 h before challenge with MSU crystals a lower PMN influx was measured (58% reduction). The occurrence of endogenous mast cell activation, in the MSU response, was validated by the observation that MSU challenge reduced by more than 90% the number of intact mast cells recovered in the peritoneal washes. Pretreatment of mice with a histamine H1 antagonist (tripolidine; 0.5 mg/kg) or a platelet-activating factor receptor antagonist (WEB2086; 10 mg/kg) significantly reduced by 50 to 60% the number of PMN recovered from the peritoneal cavities. The mol. determinants of this process of leukocyte recruitment were also investigated. Treatment of mice with an anti-CD62P or anti-CD62E monoclonal antibody (mAb; 100 μg i.v.) produced a distinct inhibition of PMN recruitment measured at 6 h, whereas only a combined administration of both monoclonal antibodies was effective in reducing by 60% the influx of PMN caused by the MSU crystals within 24 h. In conclusion, these data highlight a role for endogenous mast cells and for endothelial-derived selectins in MSU crystal-induced PMN recruitment into the peritoneal cavity, and may be useful to dissect mol. mechanism(s) which may be operating in gouty arthritis.
RE.CNT 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 47 OF 53 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 1997:634881 HCAPLUS
DN 127:288354
TI Exacerbation of adjuvant arthritis by adrenalectomy is associated with reduced leukocyte lipocortin 1
AU Yang, Yuan Hang; Hutchinson, Paul; Leech, Michelle; Morand, Eric F.
CS Centre for Inflammatory Diseases, Monash Medical Centre, Monash University, Clayton, VIC 3168, Australia
SO Journal of Rheumatology (**1997**), 24(9), 1758-1764
CODEN: JRHUA9; ISSN: 0315-162X
PB Journal of Rheumatology Publishing Co. Ltd.
DT Journal
LA English
AB Lipocortin 1 is a mediator of the antiinflammatory actions of therapeutic glucocorticoids. Endogenous glucocorticoids modulate inflammatory arthritides including rheumatoid and adjuvant arthritis (AA), but the role of lipocortin 1 in this phenomenon is not known. We studied the effects of endogenous glucocorticoids on adjuvant arthritis and leukocyte lipocortin 1 content. Adrenalectomy or sham adrenalectomy was performed 2 days before adjuvant injection in 170 g inbred Sprague-Dawley rats. Peripheral blood was obtained and disease severity assessed by Δ paw volume and clin. score 14 days later. Leukocyte subset lipocortin 1 content was determined by double labeling permeabilization flow cytometry using specific monoclonal antibodies. Lipocortin 1 fluorescence was readily detected in control rat peripheral blood cells labeled with OX-1 (pan-leukocyte), OX-19 (CD5), W3/25 (CD4), and OX-8 (CD8). Lipocortin 1 fluorescence was significantly greater in polymorphonuclear leukocytes (PMN) (RP3). Induction of AA was accompanied by significant increases in lipocortin 1 in all subsets. Sham adrenalectomy induced no significant change in AA rat leukocyte lipocortin 1. Adrenalectomy induced significant exacerbation of AA disease severity compared to sham operation (Δ paw volume 1.43 vs. 1.13 mL). Adrenalectomy was also associated with significant reduction in lipocortin 1 content in all leukocyte subsets except PMN. Leukocyte lipocortin 1 content exhibited significant neg. correlation with clin. disease severity. Endogenous glucocorticoids modulate leukocyte expression of lipocortin 1 in inflammatory disease, and reduced lipocortin 1 may be involved in the exacerbation of AA by adrenalectomy.
RE.CNT 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 48 OF 53 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 1997:435473 HCAPLUS
DN 127:159788
TI Annexins in cancer and autoimmune diseases
AU Bastian, B. C.
CS Klinik Poliklinik Hautkrankheiten, Julius-Maximilians Universitat, Wuerzburg, D-97080, Germany
SO Cellular and Molecular Life Sciences (**1997**), 53(6), 554-556
CODEN: CMLSFI; ISSN: 1420-682X
PB Birkhaeuser
DT Journal; General Review
LA English
AB A review with 44 refs. is given. Several **annexins** have been implicated in the pathogenesis of benign and malignant neoplasms of different origins. In some tumors a suppressive action of **annexins** has been shown, whereas studies of other tumors indicate an involvement of **annexins** in tumor progression. In the light of the expression of **annexins** at distinct episodes of fetal development these observations point towards a functional role of **annexins** in cellular development and differentiation. This view is supported by data that link certain **annexins** to distinct pathways of signal transduction. Auto-antibodies against several **annexins** have been detected in patients with autoimmune diseases such as systemic lupus erythematosus, rheumatoid **arthritis** and inflammatory bowel disease. Until now it is unclear whether their presence reflects a relevant pathogenetic mechanism or merely represents an unspecific expression of a raised autoimmunity in these patients.

L7 ANSWER 49 OF 53 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 1995:267972 HCAPLUS
DN 122:53428
TI Identification of a soluble Fcγ-binding molecule (annexin II) in human serum using a competitive ELISA
AU Ulvestad, Elling; Kristoffersen, Einar K.; Jensen, Tone Skeie; Matre, Roald
CS Gade Institute, University of Bergen, Bergen, N-5021, Norway
SO APMIS (**1994**), 102(9), 667-73
CODEN: APMSEL; ISSN: 0903-4641
DT Journal
LA English
AB The authors have previously produced a monoclonal antibody (mAb), B1D6, reactive with a 37 kDa placental IgG Fc-binding mol. (FcR), recently identified as annexin II. Annexin II is an intracellular mol. found in several cell types, including endothelium and monocytes. Since soluble Fc-binding mols. are of importance in the regulation of the immune response, the authors have now used B1D6 in a competitive ELISA to study levels of soluble annexin II in human sera. Soluble annexin II was detected in all sera studied. The highest levels were observed in patients with infectious mononucleosis. Gel filtration of sera revealed annexin II in fractions corresponding to a mol. weight of 40-60 kDa. In Western blot anal. a mol. of approx. 37 kDa was found. The pI of soluble annexin II was about 7.5-8 as demonstrated by chromatofocusing. Annexin II belongs to a family of phospholipid-binding mols. involved in anti-inflammatory responses, and elevated levels of annexin II in serum may be important for the suppression of an immune response.

L7 ANSWER 50 OF 53 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 1994:214821 HCAPLUS
DN 120:214821
TI The 56K autoantigen is identical to human annexin XI
AU Misaki, Yoshikata; Pruijn, Ger J. M.; van der Kemp, Annemiete W. C. M.; van Venrooij, Walther J.
CS Dep. Biochem., Univ. Nijmegen, Nijmegen, Neth.
SO Journal of Biological Chemistry (**1994**), 269(6), 4240-6
CODEN: JBCHA3; ISSN: 0021-9258
DT Journal

LA English
AB Anti-56K autoantibodies are present in sera from patients with various autoimmune diseases, predominantly in sera from patients with rheumatoid **arthritis**, systemic lupus erythematosus, or Sjogren's syndrome. To clarify the mol. structure of this autoantigen, the authors isolated a 2.0-kilobase pair cDNA clone considered to encode the full-length 56K autoantigen. The longest open reading frame encodes a 505-amino acid polypeptide, with a predicted mol. mass of 54.4 kDa. The in vitro translated protein is recognized by all anti-56K pos. patient sera tested. Antibodies affinity-purified using the bacterially expressed recombinant protein recognized the 56K autoantigen in a HeLa cell extract CDNA sequencing revealed that the 56K cDNA shares a high degree of homol. in both nucleotide (87%) and amino acid sequence (92.5%) with bovine **annexin** XI, indicating that the 56K cDNA encodes the human homolog of **annexin** XI, a member of the Ca2+-dependent phospholipid binding protein family. Anti-56K autoantibody exhibits both a cytoplasmic and a nuclear staining in immunofluorescence expts. Patients' sera recognize preferentially the N-terminal region of the protein, which is specific for 56K/**annexin** XI and not shared by other **annexins**, indicating that the autoimmune response to 56K/**annexin** XI in these patients is specific for this **annexin** family member.

L7 ANSWER 51 OF 53 USPATFULL on STN
AN 1999:128096 USPATFULL
TI Radiolabeled annexin conjugates with hexose and a chelator
IN Kasina, Sudhakar, Mercer Island, WA, United States
Reno, John M., Brier, WA, United States
Fritzberg, Alan R., Edmonds, WA, United States
Tait, Jonathan, Seattle, WA, United States
PA NeoRx Corporation, Seattle, WA, United States (U.S. corporation)
University of WA, Seattle, WA, United States (U.S. corporation)
PI US 5968477 19991019 <--
AI US 1996-690184 19960726 (8)
RLI Continuation-in-part of Ser. No. US 1994-351653, filed on 7 Dec 1994, now abandoned which is a continuation-in-part of Ser. No. US 1994-261064, filed on 16 Jun 1994, now abandoned which is a continuation-in-part of Ser. No. US 1994-185660, filed on 24 Jan 1994, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Dees, Jose G.; Assistant Examiner: Hartley, Michael G.
LREP Seed and Berry LLP
CLMN Number of Claims: 21
ECL Exemplary Claim: 1
DRWN 9 Drawing Figure(s); 9 Drawing Page(s)
LN.CNT 3660
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Radiolabeled annexin and modified annexin conjugates useful for imaging vascular thrombi are described. Methods for making and using such radiolabeled annexin conjugates are also provided.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 52 OF 53 USPATFULL on STN
AN 1999:89288 USPATFULL
TI Annexin binding protein
IN Hillman, Jennifer L., Mountain View, CA, United States
Corley, Neil C., Mountain View, CA, United States
Shah, Purvi, Sunnyvale, CA, United States
PA Incyte Pharmaceuticals, Inc., Palo Alto, CA, United States (U.S. corporation)
PI US 5932712 19990803 <--
AI US 1997-903801 19970731 (8)
DT Utility
FS Granted
EXNAM Primary Examiner: Scheiner, Toni R.; Assistant Examiner: Johnson, Nancy A.

LREP Incyte Pharmaceuticals, Inc.
CLMN Number of Claims: 8
ECL Exemplary Claim: 1,3
DRWN 7 Drawing Figure(s); 7 Drawing Page(s)
LN.CNT 2174
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention provides a human annexin binding protein (NABP-1) and polynucleotides which identify and encode NABP-1. The invention also provides expression vectors, host cells, agonists, antibodies and antagonists. The invention also provides methods for treating disorders associated with expression of NABP-1.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 53 OF 53 USPATFULL on STN
AN 1999:43184 USPATFULL
TI Membrane-bound cytokine compositions comprising GM=CSF and methods of modulating an immune response using same
IN Hoo, William Soo, Carlsbad, CA, United States
PA The Immune Response Corporation, Carlsbad, CA, United States (U.S. corporation)
PI US 5891432 19990406 <--
AI US 1997-902516 19970729 (8)
DT Utility
FS Granted
EXNAM Primary Examiner: Spector, Lorraine
LREP Campbell & Flores LLP
CLMN Number of Claims: 24
ECL Exemplary Claim: 1,13
DRWN 9 Drawing Figure(s); 7 Drawing Page(s)
LN.CNT 1917
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention provides a cellular vaccine having a membrane-bound fusion protein that includes a non-antibody immunomodulatory molecule such as GM-CSF operatively fused to a heterologous membrane attachment domain. Non-antibody immunomodulatory molecules useful in the invention include immunostimulatory and immunosuppressive molecules such as cytokines. In one embodiment, the invention provides a cellular vaccine having a membrane-bound fusion protein that includes a non-antibody immunomodulatory molecule operatively fused to a heterologous membrane attachment domain and, additionally, a disease-associated antigen or immunogenic epitope thereof. Further provided by the invention are methods of modulating an immune response against a disease-associated antigen by administering to an individual a cellular vaccine having a membrane-bound fusion protein that includes a non-antibody immunomodulatory molecule operatively fused to a heterologous membrane attachment domain.

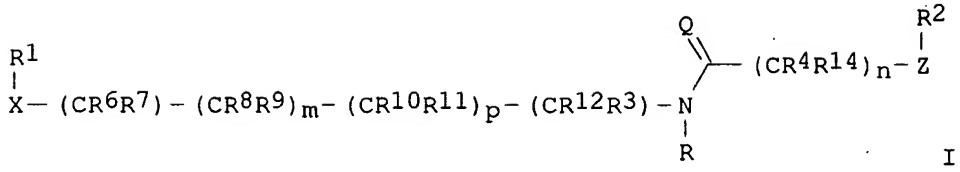
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L10 ANSWER 1 OF 15 USPATFULL on STN
AN 2005:159008 USPATFULL
TI Treatment of pancreatitis using alpha 7 receptor-binding cholinergic agonists
IN Tracey, Kevin J., Old Greenwich, CT, UNITED STATES
Wang, Hong, Havertown, PA, UNITED STATES
PA North Shore Long-Island Jewish Research Institute, Manhasset, NY, UNITED STATES (U.S. corporation)
PI US 2005137218 A1 20050623
AI US 2004-957426 A1 20040930 (10)
RLI Continuation-in-part of Ser. No. US 2003-729427, filed on 5 Dec 2003, PENDING
PRAI US 2002-431650P 20021206 (60)
DT Utility
FS APPLICATION
LREP HAMILTON, BROOK, SMITH & REYNOLDS, P.C., 530 VIRGINIA ROAD, P.O. BOX 9133, CONCORD, MA, 01742-9133, US
CLMN Number of Claims: 26
ECL Exemplary Claim: 1
DRWN 15 Drawing Page(s)
LN.CNT 1674
AB A method of treating a patient suffering from pancreatitis comprising treating said patient with a therapeutically effective amount of a cholinergic agonist selective for an α7 nicotinic receptor in an amount sufficient to decrease the amount of the proinflammatory cytokine that is released from a macrophage wherein said condition is acute pancreatitis. The compounds of the present invention include a quaternary analog of cocaine; (1-aza-bicyclo[2.2.2]oct-3-yl)-carbamic acid 1-(2-fluorophenyl)-ethyl ester; a compound of formula (I), a compound of formula (II), a compound of formula (III), a compound of formula (IV), and an oligonucleotide or mimetic capable of attenuating the symptoms of acute pancreatitis wherein the oligonucleotide or mimetic consists essentially of a sequence greater than 5 nucleotides long that is complementary to an mRNA of an α7 cholinergic receptor. The variables of formulae (I), (II), (III) and (IV) are described herein. ##STR1##

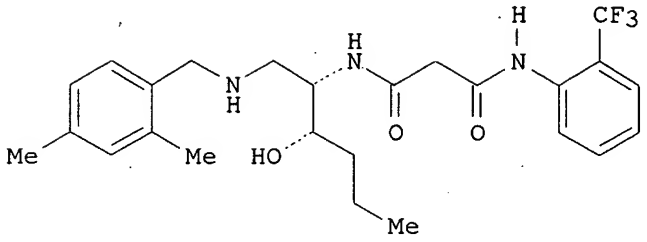
L10 ANSWER 2 OF 15 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 2004:995914 HCAPLUS
DN 141:424020
TI Preparation of malonamide derivatives as modulators of chemokine receptor activity
IN Carter, Percy
PA Bristol-Myers Squibb Company, USA
SO PCT Int. Appl., 158 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004098512	A2	20041118	WO 2004-US13453	20040430
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	US 2004235835	A1	20041125	US 2004-836032	20040429
PRAI	US 2003-467028P	P	20030501		
OS	MARPAT 141:424020				

GI



I



II

AB Monocyte chemotactic protein-1 (MCP 1) modulators I [Z = bond, CO, CONR18; Q = O, S; X = CHR16NR17; R = H, Me, Et; R1, R2 = (un)substituted C6-10 aryl, 5-10-membered heteroaryl; R3 = H, hydroxyalkyl, mercaptoalkyl, alkoxyalkyl, sulfinylalkyl, aminoalkyl, etc; R6-R12 = independently H, (un)substituted C1-6 alkyl, C2-8 alkenyl, C2-8 alkynyl, cycloalkyl, aralkyl, etc.; R3 and R12, R6 and R6, R8 and R9, R10 and R11 may form 3-6-membered carbocyclic or lactone ring; R4, R14 = independently H, F, (un)substituted C1-4 alkyl; R16-R18 = H, C1-4 alkyl, C3-6 cycloalkyl; n = 0-2; m = 0-1; p = 0-1] or pharmaceutically acceptable salt forms thereof, useful for the prevention of asthma, multiple sclerosis, artherosclerosis, and rheumatoid **arthritis** are described. Thus, amidation of N-(2-trifluoromethylphenyl)malonamic acid (preparation given) with (2S,3S)-2-amino-3-hydroxyhex-4-ynylcarbamic acid benzyl ester, followed by hydrogenation and reductive alkylation with 2,4-dimethylbenzaldehyde gave title compound II. Prepared compds. I have activity in the antagonism of MCP-1 binding to human peripheral blood mononuclear cells and in the antagonism of MCP-1-induced **calcium influx**.

L10 ANSWER 3 OF 15 USPATFULL on STN
AN 2004:261853 USPATFULL
TI Inhibition of inflammation using alpha 7 receptor-binding cholinergic agonists
IN Tracey, Kevin J., Old Greenwich, CT, UNITED STATES
Wang, Hong, Havertown, PA, UNITED STATES
PA North Shore-Long Island Jewish Research Institute, Manhasset, NY, UNITED STATES (U.S. corporation)
PI US 2004204355 A1 20041014
AI US 2003-729427 A1 20031205 (10)
PRAI US 2002-431650P 20021206 (60)
DT Utility
FS APPLICATION
LREP HAMILTON, BROOK, SMITH & REYNOLDS, P.C., 530 VIRGINIA ROAD, P.O. BOX 9133, CONCORD, MA, 01742-9133
CLMN Number of Claims: 55
ECL Exemplary Claim: 1
DRWN 11 Drawing Page(s)
LN.CNT 2175
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Methods of inhibiting release of a proinflammatory cytokine from a macrophage are provided. The methods comprise treating the macrophage with a cholinergic agonist in an amount sufficient to decrease the amount of the proinflammatory cytokine that is released from the

macrophage, wherein the cholinergic agonist is selective for an α7 nicotinic receptor. Methods for inhibiting an inflammatory cytokine cascade in a patient are also provided. The methods comprise treating the patient with a cholinergic agonist in an amount sufficient to inhibit the inflammatory cytokine cascade, wherein the cholinergic agonist is selective for an α7 nicotinic receptor. Methods for determining whether a compound is a cholinergic agonist reactive with an α7 nicotinic receptor are also provided. The methods comprise determining whether the compound inhibits release of a proinflammatory cytokine from a mammalian cell. Additionally, methods for determining whether a compound is a cholinergic antagonist reactive with an α7 nicotinic receptor are provided. These methods comprise determining whether the compound reduces the ability of a cholinergic agonist to inhibit the release of a proinflammatory cytokine from a mammalian cell. Oligonucleotides or mimetics capable of inhibiting attenuation of lipopolysaccharide-induced TNF release from a mammalian macrophage upon exposure of the macrophage to a cholinergic agonist are also provided. The oligonucleotides or mimetics consist essentially of a sequence greater than 5 nucleotides long that is complementary to an mRNA of an α7 receptor. Additionally, methods of inhibiting attenuation of TNF release from a mammalian macrophage upon exposure of the macrophage to a cholinergic agonist are provided. These methods comprise treating the macrophage with the above-described oligonucleotide or mimetic.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L10 ANSWER 4 OF 15 USPATFULL on STN
AN 2004:70691 USPATFULL
TI Methods and compositions related to modulators of annexin and cartilage homeostasis
IN Chubinskaya, Susan, Vernon Hills, IL, UNITED STATES
Hutchins, Jeff, Chapel Hill, NC, UNITED STATES
Mollenhauer, Juergen, Eisenberg, GERMANY, FEDERAL REPUBLIC OF
Tavares, Francis X., Durham, NC, UNITED STATES
Thomson, Stephen A., Durham, NC, UNITED STATES
Worley, Jennings F., Durham, NC, UNITED STATES
PI US 2004053919 A1 20040318
AI US 2003-659801 A1 20030911 (10)
RLI Division of Ser. No. US 2000-745989, filed on 21 Dec 2000, GRANTED, Pat. No. US 6649366
PRAI US 1999-173692P 19991229 (60)
DT Utility
FS APPLICATION
LREP DAVID J LEVY, CORPORATE INTELLECTUAL PROPERTY, GLAXOSMITHKLINE, FIVE MOORE DR., PO BOX 13398, RESEARCH TRIANGLE PARK, NC, 27709-3398
CLMN Number of Claims: 28
ECL Exemplary Claim: 1
DRWN 3 Drawing Page(s)
LN.CNT 1477
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention provides a method of treating a subject with arthritis or an arthritic disease or preventing arthritis or arthritic disease in a subject, comprising administering to the subject a therapeutically effective amount of an agent that attenuates annexin function. Also provided are various methods of screening for agents and genes that increase collagen synthesis, decrease collagen degradation, or reduce or delay apoptosis, and methods of using the identified agents or nucleic acids for attaining or maintaining cartilage homeostasis, promoting cartilage repair, increasing collagen synthesis, decreasing collagen degradation, or reducing or delaying apoptosis. The invention also provides methods of decreasing mineralization of vesicles derived from chondrocytes and of promoting endochondral bone growth using agents that attenuates annexin function. The present invention also provides a composition comprising isolated chondrocytes, an agent that attenuates annexin function, and collagen fragments or other means for challenging chondrocytes, including for example, collagen fragments, collagen peptides, or immune mediators.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L10 ANSWER 5 OF 15 USPATFULL on STN
AN 2004:50939 USPATFULL
TI Airway-specific trypsin-like enzymes and method of using the same
IN Eguchi, Hiroshi, Tokyo, JAPAN
Chokki, Manabu, Tokyo, JAPAN
Yamamura, Satoshi, Tokyo, JAPAN
Mita, Reiko, Tokyo, JAPAN
Masegi, Tsukio, Tokyo, JAPAN
PI US 2004038369 A1 20040226
AI US 2003-362881 A1 20030227 (10)
WO 2001-JP7349 20010828
PRAI JP 2000-257104 20000828
DT Utility
FS APPLICATION
LREP SUGHRUE MION, PLLC, 2100 PENNSYLVANIA AVENUE, N.W., WASHINGTON, DC, 20037
CLMN Number of Claims: 27
ECL Exemplary Claim: 1
DRWN 16 Drawing Page(s)
LN.CNT 4440
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The subjects of the present invention are to provide a method of screening a compound or a polypeptide which inhibits the activity of AST, or inhibits PAR activation, mucus production promotion, cell proliferation, intracellular calcium influx or EGFR pathway activation due to AST, and further to provide a method of assaying AST in vivo and in biological cells or samples.

The present invention further includes the following inventions. ASTs whose each is protein comprising the whole amino acid sequence represented by SEQ ID NO: 1 or 2 or a part thereof or a mammalian AST protein having a 66% or more homology with the amino acid sequence represented by SEQ ID NO: 1 and in whose each a propeptide moiety is bound to a trypsin-like protein moiety via a disulfide bond. Nucleic acids encoding the same. Antibodies binding to the same. A method for assaying AST by using these antibodies. Further a method of assaying the inhibitory activity of a compound or a polypeptide to be assayed against AST or PAR activation, mucus production promotion, cell proliferation, intracellular calcium influx or EGFR pathway activation due to the AST.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L10 ANSWER 6 OF 15 MEDLINE on STN DUPLICATE 1
AN 2004623194 MEDLINE
DN PubMed ID: 15593223
TI CC and CXC chemokine receptors mediate migration, proliferation, and matrix metalloproteinase production by fibroblast-like synoviocytes from rheumatoid arthritis patients.
AU Garcia-Vicuna Rosario; Gomez-Gaviro Maria Victoria; Dominguez-Luis Maria Jesus; Pec Martina K; Gonzalez-Alvaro Isidoro; Alvaro-Gracia Jose Maria; Diaz-Gonzalez Federico
CS Hospital Universitario de la Princesa, Universidad Autonoma de Madrid, Madrid, Spain.
SO Arthritis and rheumatism, (2004 Dec) 50 (12) 3866-77.
Journal code: 0370605. ISSN: 0004-3591.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 200501
ED Entered STN: 20041220
Last Updated on STN: 20050114
Entered Medline: 20050113
AB OBJECTIVE: To explore the potential involvement of the chemokine system in synoviocyte-mediated tissue destruction in rheumatoid **arthritis** (RA), we studied the expression profile of chemokine receptors and their

function in the migration, proliferation, and matrix metalloproteinase (MMP) production of cultured fibroblast-like synoviocytes (FLS) from RA patients. METHODS: The presence of CC and CXC chemokine receptors on cultured FLS was studied at the messenger RNA (mRNA) level by reverse transcriptase-polymerase chain reaction and at the cell surface expression level by flow cytometry. Variations in cytosolic **calcium influx** induced by chemokine stimulation were assessed by flow cytometry on Fura Red-preloaded FLS. Two-compartment transwell chambers were used for FLS chemotaxis assays. Cell growth was measured by a fluorescence-based proliferation assay. Gelatinase and collagenase activities were determined by a fibril degradation assay and zymography. RESULTS: FLS constitutively expressed the receptors CCR2, CCR5, CXCR3, and CXCR4, both at the cell surface and mRNA levels, but failed to express CCR3 and CCR6. Significant intracytosolic **calcium influx** was observed on FLS challenged with monocyte chemotactic protein 1 (MCP-1), stromal cell-derived factor lalpha (SDF-1alpha), and interferon-inducible protein 10 (IP-10). Stimulation with MCP-1, SDF-1alpha, IP-10, and monokine induced by interferon-gamma enhanced the migration and proliferation of FLS. These chemokines, in addition to RANTES, increased in a dose- and time-dependent manner the gelatinase and collagenase activities in cell-free supernatants of cultured FLS. Interestingly, the chemokine-mediated up-regulation of MMP activities was significantly abrogated by the presence of anti-interleukin-1beta, but not anti-tumor necrosis factor alpha, blocking antibodies. CONCLUSION: These data suggest that through modulation of the migration, proliferation, and MMP production by FLS, the chemokine system may play a more direct role in the destructive phase of RA than is currently suspected, and thus emphasize the relevance of chemokines and their receptors as potential therapeutic targets in this disease.

L10 ANSWER 7 OF 15 USPATFULL on STN
AN 2003:101072 USPATFULL
TI Transgenic mammals having human Ig loci including plural Vh and Vk regions and antibodies produced therefrom
IN Jakobovits, Aya, Menlo Park, CA, UNITED STATES
Kucherlapati, Raju, Darien, CT, UNITED STATES
Klapholz, Susan, Stanford, CA, UNITED STATES
Mendez, Michael J., El Granada, CA, UNITED STATES
Green, Larry, San Francisco, CA, UNITED STATES
PI US 2003070185 A1 20030410
AI US 2002-78958 A1 20020219 (10)
RLI Continuation of Ser. No. US 1996-759620, filed on 3 Dec 1996, ABANDONED
DT Utility
FS APPLICATION
LREP FISH & NEAVE, 1251 AVENUE OF THE AMERICAS, 50TH FLOOR, NEW YORK, NY, 10020-1105
CLMN Number of Claims: 28
ECL Exemplary Claim: 1
DRWN 53 Drawing Page(s)
LN.CNT 2295
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to transgenic non-human animals that are engineered to contain human immunoglobulin gene loci. In particular, animals in accordance with the invention possess human Ig loci that include plural variable (V.sub.H and Vκ) gene regions. Advantageously, the inclusion of plural variable region genes enhances the specificity and diversity of human antibodies produced by the animal. Further, the inclusion of such regions enhances and reconstitutes B-cell development to the animals, such that the animals possess abundant mature B-cells secreting extremely high affinity antibodies.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

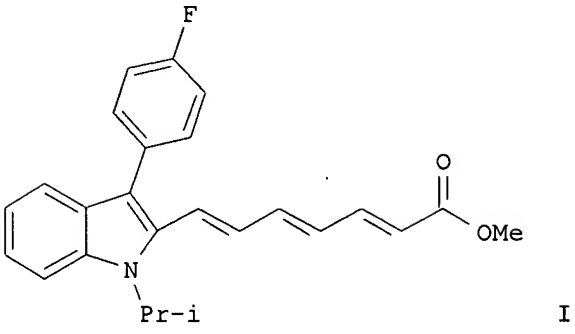
L10 ANSWER 8 OF 15 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
AN 2004:198402 BIOSIS
DN PREV200400198961
TI Calcium binding proteins in central sensitization.

AU Vadaszova, A. [Reprint Author]; Spicarova, D. [Reprint Author]; Palecek, J. [Reprint Author]
CS Czech Acad. of Sci., Inst. of Physiology, Prague, Czech Republic
SO Society for Neuroscience Abstract Viewer and Itinerary Planner, (2003) Vol. 2003, pp. Abstract No. 383.12. http://sfn.scholarone.com. e-file. Meeting Info.: 33rd Annual Meeting of the Society of Neuroscience. New Orleans, LA, USA. November 08-12, 2003. Society of Neuroscience.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 14 Apr 2004
Last Updated on STN: 14 Apr 2004
AB Sensitization of spinal cord neurons may play an important role in chronic pain states. Increased **calcium influx** and/or its release from internal stores are considered to be one of the key mechanisms in the sensitization process. The physiological effect of the Ca++ is dependent on activation of Ca dependent secondary messengers and is thus limited by the amplitude of the concentration change and the distance of diffusion from the source of the Ca++ (e.g. by the size of the Ca micro-domain). Calcium binding proteins (CBP) represent one of the key factors in the calcium buffering properties of the cells and have thus high impact on the size of the Ca micro-domain size after Ca++ influx. In this study the role of CBP in sensitization of spinothalamic tract (STT) neurons after peripheral inflammation was examined. STT neurons were retrogradely labeled by fluorescent dextrans injected in the thalamus of control and **arthritic** rats. The animals were injected with a mixture of kaolin and carrageenan into the knee joint for induction of experimental **arthritis**. Presence of calcium binding proteins (calretinin-CR, parvalbumin-PA, calbindin-CA) in STT neurons was assessed immuno-histochemically in fixed spinal cord slices from lumbar segments L4-6. While CR was present in STT neurons under both control and experimental conditions, the number of STT neurons positively labeled for PA and CB increased after peripheral inflammation. Our results suggest that CBP may play an important role in the sensitization of spinal neurons that are involved in pain transmission.

L10 ANSWER 9 OF 15 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 2002:927240 HCAPLUS
DN 138:11405
TI Store operated calcium influx inhibitors and methods of use
IN Parks, Thomas P.; Baker, Don R.
PA Cellegy Pharmaceuticals, Inc., USA
SO PCT Int. Appl., 127 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2002096416	A1	20021205	WO 2002-US17112	20020531
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2445712	AA	20021205	CA 2002-2445712	20020531
US 2003114353	A1	20030619	US 2002-160977	20020531
US 6699886	B2	20040302		
EP 1390030	A1	20040225	EP 2002-734606	20020531
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
US 2004106537	A1	20040603	US 2003-670665	20030924
US 6869961	B2	20050322		

PRAI US 2001-295124P P 20010531
US 2001-295129P P 20010531
US 2002-160977 A1 20020531
WO 2002-US17112 W 20020531
OS MARPAT 138:11405
GI



I

AB The present invention provides store operated calcium influx inhibitor compds., pharmaceutical compns., and methods of use. The compds. are useful for treating an inflammatory disease or treating an inflammatory reaction. Preferably, compds., compns. and methods of this invention are used for treatment of inflammatory skin, pulmonary, musculoskeletal, and gastrointestinal diseases, as well as autoimmune disorders, transplantation treatment, and osteoporosis. The compds. of the present invention are preferably store-operated calcium influx (SOC) inhibitors which inhibit calcium uptake into non-excitable cells in response to stimulus-mediated depletion of intracellular calcium storage pools. The SOC inhibitors preferably inhibit one or more of the following: calcium-dependent activation of nuclear factor of activated T cells, nuclear factor kB, the stress kinases c-Jun N-terminal kinase and exocytosis, resulting in the release or elaboration of inflammatory mediators. Examples of SOC inhibitors are statins in the δ-lactone form such as lovastatin, mevastatin and simvastatin, as well as the novel compound, I. Examples of enema, suppository, and controlled-release tablet formulations are given.
RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 10 OF 15 USPATFULL on STN
AN 2002:99457 USPATFULL
TI Methods and compositions related to modulators of annexin and cartilage homeostasis
IN Chubinskaya, Susan, Vernon Hills, IL, UNITED STATES
Hutchins, Jeff, Chapel Hill, NC, UNITED STATES
Mollenhauer, Juergen, Eisenberg, GERMANY, FEDERAL REPUBLIC OF
Tavares, Francis X., Durham, NC, UNITED STATES
Thomson, Stephen A., Durham, NC, UNITED STATES
Worley, Jennings F., Durham, NC, UNITED STATES
PI US 2002052358 A1 20020502
US 6649366 B2 20031118
AI US 2000-745989 A1 20001221 (9)
PRAI US 1999-173692P 19991229 (60)
DT Utility
FS APPLICATION
LREP DAVID J LEVY, VP INTELLECTUAL PROPERTY, GLAXO WELLCOME INC, GLOBAL INTELLECTUAL PROPERTY, FIVE MOORE DR, PO BOX 13398, RESEARCH TRIANGLE PARK, NC, 27709-3398
CLMN Number of Claims: 67
ECL Exemplary Claim: 1
DRWN 3 Drawing Page(s)

LN.CNT 1621
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention provides a method of treating a subject with arthritis or an arthritic disease or preventing arthritis or arthritic disease in a subject, comprising administering to the subject a therapeutically effective amount of an agent that attenuates annexin function. Also provided are various methods of screening for agents and genes that increase collagen synthesis, decrease collagen degradation, or reduce or delay apoptosis, and methods of using the identified agents or nucleic acids for attaining or maintaining cartilage homeostasis, promoting cartilage repair, increasing collagen synthesis, decreasing collagen degradation, or reducing or delaying apoptosis. The invention also provides methods of decreasing mineralization of vesicles derived from chondrocytes and of promoting endochondral bone growth using agents that attenuates annexin function. The present invention also provides a composition comprising isolated chondrocytes, an agent that attenuates annexin function, and collagen fragments or other means for challenging chondrocytes, including for example, collagen fragments, collagen peptides, or immune mediators.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L10 ANSWER 11 OF 15 MEDLINE on STN DUPLICATE 2
AN 2002221130 MEDLINE
DN PubMed ID: 11958824
TI Interferon-gamma-induced **calcium influx** in T lymphocytes of multiple sclerosis and rheumatoid **arthritis** patients: a complementary mechanism for T cell activation?.
AU Buntinx Mieke; Ameloot Marcel; Steels Paul; Janssen Paul; Medaer Robert; Geusens Piet; Raus Jef; Stinissen Piet
CS Biomedisch Onderzoeksinstituut, Limburgs Universitair Centrum and School of Life Sciences, Transnational University Limburg, Universitaire Campus gebouw A, B-3590 Diepenbeek, Belgium.
SO Journal of neuroimmunology, (2002 Mar) 124 (1-2) 70-82.
Journal code: 8109498. ISSN: 0165-5728.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200205
ED Entered STN: 20020418
Last Updated on STN: 20020503
Entered Medline: 20020502
AB Autoreactive T lymphocytes are considered to play a crucial role in orchestrating a chronic inflammation in the central nervous system (CNS) of multiple sclerosis (MS) patients and in the joints of rheumatoid arthritis (RA) patients. However, it has been suggested that the majority of T cells in the immune infiltrate are nonspecifically recruited into the CNS and into the inflamed joint. In addition, several lines of evidence suggest an important role for interferon-gamma (IFN-gamma) in the pathogenesis of MS and RA. We have studied whether peripheral blood T cells from patients with autoimmune diseases are more susceptible to activation in the presence of IFN-gamma. The results indicate that IFN-gamma mediates a sustained elevated [Ca(2+)](i) in T cells of (active) MS and RA patients as compared to healthy controls and patients with common viral infections. No [Ca(2+)](i) increase was observed in Ca(2+)-free medium, excluding an effect of IFN-gamma on Ca(2+)-release from intracellular stores. Although the IFN-gamma-activated Ca(2+)-influx is insufficient to induce T cell proliferation in vitro, our data indicate a significantly augmented proliferation in response to suboptimal doses of PHA in the presence of IFN-gamma. This study suggests that the IFN-gamma-induced Ca(2+)-influx can act as a complementary mechanism in the activation of blood T lymphocytes from MS and RA patients.

L10 ANSWER 12 OF 15 USPATFULL on STN
AN 2000:95022 USPATFULL
TI 4-substituted beta-carbolines and analogs thereof
IN Miao, Clara K, Easton, CT, United States

Potocki, Ian F., Danbury, CT, United States
Snow, Roger J., Danbury, CT, United States
Hargrave, Karl D., Brookfield, CT, United States
Parks, Thomas P., Ridgefield, CT, United States
PA Boehringer Ingelheim Pharmaceuticals, Inc., Ridgefield, CT, United States (U.S. corporation)
PI US 6093723 20000725
AI US 1997-908211 19970808 (8)
PRAI US 1996-23650P 19960809 (60)
DT Utility
FS Granted
EXNAM Primary Examiner: Huang, Evelyn Mei
LREP Raymond, Robert P., Bottino, Anthony P., Stempel, Alan R.
CLMN Number of Claims: 24
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1560
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention relates to 4-substituted β-carbolines and β-carboline analogs that inhibit Ca.sup.+2 influx and interleukin-2 (IL-2) production. The 4-substituted β-carbolines and β-carboline analogs of this invention are represented by formula (I): ##STR1## wherein Q, n, R, R', R" and R.sub.1 -R.sub.4 are as defined herein. This invention also relates to methods for producing β-carbolines. Because of their selective immunomodulating properties, the compounds and pharmaceutical compositions of this invention are particularly well suited for preventing and treating immune disorders, including autoimmune disease, inflammatory disease, organ transplant rejection and other disorders associated with IL-2 mediated immune response.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L10 ANSWER 13 OF 15 MEDLINE on STN DUPLICATE 3
AN 2000437211 MEDLINE
DN PubMed ID: 10770925
TI Identification of the binding site for a novel class of CCR2b chemokine receptor antagonists: binding to a common chemokine receptor motif within the helical bundle.
AU Mirzadegan T; Diehl F; Ebi B; Bhakta S; Polsky I; McCarley D; Mulkins M; Weatherhead G S; Lapierre J M; Dankwardt J; Morgans D Jr; Wilhelm R; Jarnagin K
CS Roche Bioscience, Palo Alto, CA 94304, USA.. tara.mirzadegan@roche.com
SO Journal of biological chemistry, (2000 Aug 18) 275 (33) 25562-71.
Journal code: 2985121R. ISSN: 0021-9258.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200009
ED Entered STN: 20000928
Last Updated on STN: 20000928
Entered Medline: 20000921
AB Monocyte chemoattracant-1 (MCP-1) stimulates leukocyte chemotaxis to inflammatory sites, such as rheumatoid **arthritis**, atherosclerosis, and asthma, by use of the MCP-1 receptor, CCR2, a member of the G-protein-coupled seven-transmembrane receptor superfamily. These studies identified a family of antagonists, spiropiperidines. One of the more potent compounds blocks MCP-1 binding to CCR2 with a K(d) of 60 nm, but it is unable to block binding to CXCR1, CCR1, or CCR3. These compounds were effective inhibitors of chemotaxis toward MCP-1 but were very poor inhibitors of CCR1-mediated chemotaxis. The compounds are effective blockers of MCP-1-driven inhibition of adenylate cyclase and MCP-1- and MCP-3-driven cytosolic **calcium influx**; the compounds are not agonists for these pathways. We showed that glutamate 291 (Glu(291)) of CCR2 is a critical residue for high affinity binding and that this residue contributes little to MCP-1 binding to CCR2. The basic nitrogen present in the spiropiperidine compounds may be the interaction

partner for Glu(291), because the basicity of this nitrogen was essential for affinity; furthermore, a different class of antagonists, a class that does not have a basic nitrogen (2-carboxypyrroles), were not affected by mutations of Glu(291). In addition to the CCR2 receptor, spiropiperidine compounds have affinity for several biogenic amine receptors. Receptor models indicate that the acidic residue, Glu(291), from transmembrane-7 of CCR2 is in a position similar to the acidic residue contributed from transmembrane-3 of biogenic amine receptors, which may account for the shared affinity of spiropiperidines for these two receptor classes. The models suggest that the acid-base pair, Glu(291) to piperidine nitrogen, anchors the spiropiperidine compound within the transmembrane ovoid bundle. This binding site may overlap with the space required by MCP-1 during binding and signaling; thus the small molecule ligands act as antagonists. An acidic residue in transmembrane region 7 is found in most chemokine receptors and is rare in other serpentine receptors. The model of the binding site may suggest ways to make new small molecule chemokine receptor antagonists, and it may rationalize the design of more potent and selective antagonists.

L10 ANSWER 14 OF 15 MEDLINE on STN DUPLICATE 4
AN 1998175977 MEDLINE
DN PubMed ID: 9507015
TI Requirements of focal adhesions and calcium fluxes for interleukin-1-induced ERK kinase activation and c-fos expression in fibroblasts.
AU Lo Y Y; Luo L; McCulloch C A; Cruz T F
CS Samuel Lunenfeld Research Institute, Mount Sinai Hospital, Toronto, Ontario M5G 1X5, Canada.
SO Journal of biological chemistry, (1998 Mar 20) 273 (12) 7059-65.
Journal code: 2985121R. ISSN: 0021-9258.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199804
ED Entered STN: 19980422
Last Updated on STN: 19980422
Entered Medline: 19980416
AB Interleukin-1 (IL-1) is an important inflammatory mediator and plays a central role in the destruction of connective tissue matrices in diseases such as **arthritis** and periodontitis. It is well established that IL-1 activation of the mitogen-activated protein (MAP) kinase pathway and induction of c-fos expression is a required step in the induction of matrix metalloproteinase expression involved in tissue degradation. Previous studies in our laboratory showed that IL-1-induced calcium flux is dependent on focal adhesion formation, suggesting a matrix-dependent restriction system for IL-1 signaling. Therefore, in the present study, we examined the consequences of this restriction on IL-1-mediated activation of the MAP kinase family and on c-fos expression. Treatment of human gingival fibroblasts with IL-1 activated extracellular signal-regulated kinases (ERK), c-Jun N-terminal kinase (JNK), and p38 kinase activity and induced c-fos expression in a dose- and time-dependent fashion. Plating cells on poly-L-lysine prevented focal adhesion formation, eliminated IL-1-induced **calcium influx**, abolished ERK stimulation, and blocked c-fos expression. Cells in suspension and hence with no suitable substratum for focal adhesion formation also showed no ERK activation or enhanced c-fos expression in response to IL-1. In contrast, eliminating focal adhesion formation or calcium depletion in cells plated on fibronectin had no effect on IL-1 stimulation of JNK and p38 kinases, demonstrating that their activation was mediated through pathways independent of focal adhesions and calcium. Calcium depletion abolished IL-1-induced calcium uptake, ERK activation, and c-fos expression. The focal adhesion dependence of IL-1-induced ERK activation and c-fos expression could be circumvented in cells plated on poly-L-lysine by simultaneous incubation with IL-1 and the calcium ionophore ionomycin. In transfection studies, IL-1 stimulation of serum responsive element (SRE) transcriptional activity was dependent on the presence of extracellular calcium. This is consistent with a requirement

for calcium in the activation of ERKs and their involvement in the induction of c-fos expression through the SRE site on the 5' promoter of the c-fos gene. Our results demonstrate that in cells attached to substrates by focal adhesions, IL-1-mediated calcium flux is required for ERK activation and c-fos expression but not for JNK or p38 activation. We conclude that cellular interactions with the extracellular matrix play an important role in restricting ERK and c-fos-dependent processes.

L10 ANSWER 15 OF 15 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
AN 1993:39833 BIOSIS
DN PREV199344016683
TI Inhibition by remission inducing drugs (RID) of **calcium influx** by neutrophils, human synovial cells and human chondrocytes: The mechanisms of action of RID in rheumatoid **arthritis** (RA) patients.
AU Shingu, Masao; Nobunaga, Masshi
CS Med. Inst. Bioregul., Kyushu Univ. 69, Beppu 874, Japan
SO Arthritis and Rheumatism, (1992) Vol. 35, No. 9 SUPPL., pp. S308. Meeting Info.: 56th Annual Scientific Meeting of the American College of Rheumatology, Atlanta, Georgia, USA, October 11-15, 1992. ARTHRITIS RHEUM. CODEN: ARHEAW. ISSN: 0004-3591.
DT Conference; (Meeting)
LA English
ED Entered STN: 4 Jan 1993
Last Updated on STN: 4 Jan 1993

L14 ANSWER 1 OF 41 MEDLINE on STN
AN 2005350900 IN-PROCESS
DN PubMed ID: 16002730
TI A Non-Glycosaminoglycan-Binding Variant of CC Chemokine Ligand 7 (Monocyte Chemoattractant Protein-3) Antagonizes Chemokine-Mediated Inflammation.
AU Ali Simi; Robertson Helen; Wain Julie H; Isaacs John D; Malik Ghada; Kirby John A
CS The Applied Immunobiology and Transplantation Research Group and The Musculoskeletal Research Group, Medical School, University of Newcastle, Newcastle upon Tyne, United Kingdom.
SO Journal of immunology (Baltimore, Md. : 1950), (2005 Jul 15) 175 (2) 1257-66.
Journal code: 2985117R. ISSN: 0022-1767.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS NONMEDLINE; IN-DATA-REVIEW; IN-PROCESS; NONINDEXED; Abridged Index Medicus Journals; Priority Journals
ED Entered STN: 20050709
Last Updated on STN: 20050709
AB A non-glycosaminoglycan (GAG)-binding variant of the pleiotropic chemokine CCL7 was generated by mutating to alanine the basic (B) amino acids within an identified (44)BXBXXB(49) GAG-binding motif. Unlike wild-type (wt) CCL7, the mutant sequence had no affinity for heparin. However, the mutant retained a normal affinity for CCR1, CCR2b, and CCR3, and produced a normal **calcium flux** in mononuclear leukocytes. Both the wt and mutant proteins elicited an equal leukocyte chemotactic response within a solute diffusion gradient but, unlike the wt protein, the mutant failed to stimulate cell migration across a model endothelium. The number of leukocytes recruited to murine air pouches by the mutant sequence was lower than that recruited by wt CCL7. Furthermore, the presence of a mixture of a mutant and wt CCL7 within the air pouch elicited no significant cell accumulation. Cell recruitment also failed using a receptor-sharing mixture of mutant CCL7 and wt CCL5 or a nonreceptor sharing mixture of mutant CCL7 and wt CXCL12. The potential of the mutant sequence to modulate inflammation was confirmed by demonstration of its ability to inhibit the chemotactic response generated in vitro by synovial fluid from patients with active rheumatoid **arthritis**. A further series of experiments suggested that the non-GAG-binding mutant protein could potentially induce receptor desensitization before, and at a site remote from, any physiological recognition of GAG-bound chemokines. These data demonstrate that GAG binding is required for chemokine-driven inflammation in vivo and also suggest that a non-GAG-binding chemokine receptor agonist can inhibit the normal vectorial leukocyte migration mediated by chemokines.

L14 ANSWER 2 OF 41 MEDLINE on STN
AN 2004479269 MEDLINE
DN PubMed ID: 15382150
TI Fluorescent CXCL12AF647 as a novel probe for nonradioactive CXCL12/CXCR4 cellular interaction studies.
AU Hatse Sigrid; Princen Katrien; Liekens Sandra; Vermeire Kurt; De Clercq Erik; Schols Dominique
CS Laboratory of Virology and Chemotherapy, Rega Institute for Medical Research, Katholieke Universiteit Leuven, Minderbroedersstraat 10, B-3000 Leuven, Belgium.. sigrid.hatse@rega.kuleuven.ac.be
SO Cytometry A, (2004 Oct) 61 (2) 178-88.
Journal code: 101235694. ISSN: 1552-4922.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200503
ED Entered STN: 20040928
Last Updated on STN: 20050322
Entered Medline: 20050321
AB BACKGROUND: Chemokines drive the migration of leukocytes via interaction

with specific G protein-coupled 7-transmembrane receptors. The chemokine ligand/receptor pair stromal cell-derived factor-1 (SDF-1, CXCL12)/CXCR4 is gaining increasing interest because of its involvement in the metastasis of several types of cancer and in certain inflammatory autoimmune disorders such as rheumatoid **arthritis**. In addition, CXCR4 serves as an important coreceptor for cellular entry of T-tropic strains of human immunodeficiency virus (HIV). Therefore, potent and specific CXCR4 antagonists may have therapeutic potential as anti-HIV, anti-cancer, and anti-inflammatory drugs. METHODS AND RESULTS: Chemokine receptor antagonists can be identified by their ability to inhibit ligand binding to the receptor protein. Until now, chemokine binding assays were mostly performed with radiolabeled chemokine ligands such as [(125)I]CXCL12. To overcome the practical problems associated with such radioactive chemokine binding assays, we have developed a flow cytometric technique using a new, commercially available Alexa Fluor 647 conjugate of CXCL12 (CXCL12(AF647)). **Calcium flux**, chemotaxis, and p44/42 mitogen-activated protein kinase phosphorylation assays showed that the agonistic activity of the fluorescent CXCL12 was unchanged as compared with that of unlabeled CXCL12. Human T-lymphoid (CXCR4(+)) SupT1 cells and CXCR4-transfected, but not CCR5- or CXCR3-transfected, human astroglioma U87.CD4 cells specifically bound CXCL12(AF647) in a concentration-dependent manner. Unlabeled CXCL12 and the well-known CXCR4 inhibitors, AMD3100 and T22, blocked the binding of CXCL12(AF647) to SupT1 cells with 50% inhibitory concentrations of 92, 13, and 8 ng/ml, respectively. We have also used this method to evaluate CXCL12 binding and CXCR4 expression level in different subsets of human peripheral blood mononuclear cells. CONCLUSION: CXCL12(AF647) is a valuable, more convenient alternative for [(125)I]CXCL12 in ligand/receptor interaction studies.

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L14 ANSWER 3 OF 41 MEDLINE on STN
AN 2004139874 MEDLINE
DN PubMed ID: 15033519
TI Development of a microplate bioassay for monocyte chemoattractant protein-1 based on activation of p44/42 mitogen-activated protein kinase.
AU Hirata Terra Juliana; Montano Irene; Schilb Alain; Millward Thomas A
CS Biotechnology Development, Novartis Pharma AG, CH-4002 Basel, Switzerland.
SO Analytical biochemistry, (2004 Apr 1) 327 (1) 119-25.
Journal code: 0370535. ISSN: 0003-2697.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200411
ED Entered STN: 20040323
Last Updated on STN: 20041102
Entered Medline: 20041101
AB Monocyte chemoattractant protein-1 (MCP-1) is a potential therapeutic target for the treatment of several inflammatory conditions, including rheumatoid **arthritis** and chronic obstructive pulmonary disease. Current cell-based assays for MCP-1 use monocyte chemotaxis or **calcium flux** as a readout. Here, we describe an alternative bioassay based on MCP-1-induced phosphorylation of the mitogen-activated protein kinases (MAPK) p44 (ERK1) and p42 (ERK2). Adherent cells expressing the MCP-1 receptor CCR2B are treated with MCP-1 in 96-well plates in the presence or absence of inhibitors, fixed and permeabilized with methanol, and then probed with a monoclonal antibody that selectively recognizes the doubly phosphorylated form of p44/42 MAPK. Bound antibody is detected with a secondary antibody-peroxidase conjugate and a chromogenic substrate. The phosphorylation of p44/42 MAPK as detected in this assay peaks after 3-5 min of MCP-1 treatment, and the concentration of MCP-1 required for half-maximal p44/42 MAPK phosphorylation is 1-3 nM. MCP-1-induced phosphorylation of p44/42 MAPK is dependent upon the expression of CCR2B. The assay can be used for screening and characterization of small molecule inhibitors and antibodies blocking the binding of MCP-1 to its receptor. Since the assay is rapid and simple, it may represent a useful alternative to chemotaxis or

calcium mobilization assays for the analysis of MCP-1 inhibitors.

L14 ANSWER 4 OF 41 MEDLINE on STN
AN 2002461948 MEDLINE
DN PubMed ID: 12220670
TI Chemokine receptor inhibition by AMD3100 is strictly confined to CXCR4.
AU Hatse Sigrid; Princen Katrien; Bridger Gary; De Clercq Erik; Schols Dominique
CS Laboratory of Virology and Chemotherapy, Rega Institute for Medical Research, Katholieke Universiteit Leuven, Minderbroedersstraat 10, B-3000, Leuven, Belgium.. sigrid.hatse@rega.kuleuven.ac.be
SO FEBS letters, (2002 Sep 11) 527 (1-3) 255-62.
Journal code: 0155157. ISSN: 0014-5793.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200211
ED Entered STN: 20020911
Last Updated on STN: 20021213
Entered Medline: 20021108
AB This study was undertaken to demonstrate the unique specificity of the chemokine receptor CXCR4 antagonist AMD3100. **Calcium flux** assays with selected chemokine/cell combinations, affording distinct chemokine receptor specificities, revealed no interaction of AMD3100 with any of the chemokine receptors CXCR1 through CXCR3, or CCR1 through CCR9. In contrast, AMD3100 potently inhibited CXCR4-mediated **calcium** signaling and chemotaxis in a concentration-dependent manner in different cell types. Also, AMD3100 inhibited stromal cell-derived factor (SDF)-1-induced endocytosis of CXCR4, but did not affect phorbol ester-induced receptor internalization. Importantly, AMD3100 by itself was unable to elicit intracellular **calcium** fluxes, to induce chemotaxis, or to trigger CXCR4 internalization, indicating that the compound does not act as a CXCR4 agonist. Specific small-molecule CXCR4 antagonists such as AMD3100 may play an important role in the treatment of human immunodeficiency virus infections and many other pathological processes that are dependent on SDF-1/CXCR4 interactions (e.g. rheumatoid **arthritis**, atherosclerosis, asthma and breast cancer metastasis).

L14 ANSWER 5 OF 41 MEDLINE on STN
AN 2000065743 MEDLINE
DN PubMed ID: 10598684
TI A coculture model of synoviocytes and bone for the evaluation of potential arthritis therapies.
AU Moe S M; Bailey A M
CS Department of Medicine, Indiana University Medical Center, Wishard Memorial Hospital, Indianapolis 46202, USA.. smoe@iupui.edu
NC AR011946 (NIAMS)
SO Journal of pharmacological and toxicological methods, (1999 Apr-Jun) 41 (2-3) 127-34.
Journal code: 9206091. ISSN: 1056-8719.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Space Life Sciences
EM 200001
ED Entered STN: 20000114
Last Updated on STN: 20000114
Entered Medline: 20000104
AB OBJECTIVE: To evaluate the symbiotic relationship between musculoskeletal cells in the intact joint utilizing a coculture system and to determine if the model can be utilized to evaluate potential treatments for articular diseases. METHODS: Two neonatal mouse calvariae were placed on steel supports on a monolayer of rabbit synovial fibroblasts, and net **calcium flux**, bone cell activity, and undecalcified histology were determined at 6, 24, and 48 h. To determine if the model was predictive of response to known therapies for articular disease, the

coculture was incubated in the presence and absence of indomethacin or doxycycline, and the net **calcium flux** was measured. RESULTS: The coincubation of calvariae with synoviocytes led to a fivefold increase in net **calcium** efflux compared to calvariae alone. The concentration in the media of the osteoblastic enzyme alkaline phosphatase increased at 6 h but decreased thereafter, whereas the concentration of osteoclastic enzyme beta-glucuronidase increased with time. Undecalcified bone histology revealed progressive demineralization and an increase in the number of osteoclasts in calvariae incubated with synoviocytes compared to calvariae alone. Both indomethacin and doxycycline inhibited **calcium flux** from cocultures but the predominant effect of doxycycline was on the synoviocyte whereas the predominant effect of indomethacin was on bone. CONCLUSION: The coincubation of synoviocytes with calvariae led to an increase in bone mineral dissolution with time. This effect could be partially inhibited by known treatments for rheumatoid **arthritis**. Thus, the coculture model may simulate certain aspects of the in vivo processes relevant to rheumatoid **arthritis**. This model should prove useful for the study of potential therapies for inflammatory **arthritis** and distinguish between effects of these therapies on different cellular components of the joint.

L14 ANSWER 6 OF 41 MEDLINE on STN
AN 96187846 MEDLINE
DN PubMed ID: 8603428
TI The effect of minocycline in rat models of inflammatory **arthritis** : correlation of **arthritis** suppression with enhanced T cell **calcium flux**.
AU Sewell K L; Breedveld F; Furrie E; O'Brien J; Brinckerhoff C; Dynesius-Trentham R; Nosaka Y; Trentham D E
CS Department of Medicine, Beth Israel Hospital, Boston, Massachusetts 02215, USA.
NC AG08812 (NIA)
AR38819 (NIAMS)
SO Cellular immunology, (1996 Feb 1) 167 (2) 195-204.
Journal code: 1246405. ISSN: 0008-8749.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199605
ED Entered STN: 19960524
Last Updated on STN: 19960524
Entered Medline: 19960515
AB Adjuvant and collagen arthritis in the rat are widely accepted T-cell-dependent counterparts of rheumatoid arthritis and were used to examine the antiinflammatory properties of minocycline. Administration of oral minocycline, a semisynthetic tetracycline, significantly decreased ($P < 0.01$) the incidence of arthritis in both models. In vivo exposure to minocycline also significantly increased the percentage of splenocytes exhibiting a rise in free intracellular calcium concentration ([Ca2+]i) following concanavalin A stimulation ($P < 0.05$ in adjuvant and $P < 0.01$ in collagen). This enhancement was mitogen dose-dependent and supported exclusively by extracellular Ca2+. Resting [Ca2+]i levels were unaffected by minocycline and predominantly the CD4+ subset was involved. No changes were observed in weight, IgG antibodies to collagen, synoviocyte release of collagenase and prostaglandin E2, acute inflammation in an air-pouch system, or cell surface expression of activation markers (interleukin-2 and transferrin receptors) by splenocytes or lymph node cells. As a controlled [Ca2+]i rise is a critical event in normal T cell activation, minocycline's antiarthritic profile in vivo may relate to perturbed Ca2+ influx during T cell activation, an alteration that could promote the development of clinical tolerance to otherwise arthritogenic stimuli.

L14 ANSWER 7 OF 41 MEDLINE on STN
AN 93295126 MEDLINE
DN PubMed ID: 1305681
TI Piroxicam and other cyclooxygenase inhibitors: potential for cancer

chemoprevention.
AU Earnest D L; Hixson L J; Alberts D S
CS Department of Medicine, University of Arizona, Tucson 85724.
NC P01 CA41108 (NCI)
SO Journal of cellular biochemistry. Supplement, (1992) 16I 156-66. Ref: 54
Journal code: 8207539. ISSN: 0733-1959.
CY United States
DT (CLINICAL TRIAL)
(CLINICAL TRIAL, PHASE II)
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 199307
ED Entered STN: 19930806
Last Updated on STN: 19930806
Entered Medline: 19930722
AB Piroxicam is a nonsteroidal anti-inflammatory drug (NSAID) widely used for treatment of inflammatory **arthritis**. Recent experimental and clinical studies suggest that piroxicam, as well as other NSAIDs, may be useful for chemoprevention of colon cancer. While there is less information regarding NSAIDs for chemoprevention of urinary bladder malignancy, there are compelling data which suggest that this should be evaluated. A major effect of NSAIDs is inhibition of cyclooxygenase, the rate-limiting enzyme for conversion of arachidonic acid to important signal molecules, including prostaglandins, which profoundly affect cellular functions in many tissues. The initial enzyme reaction leading to formation of prostaglandin H can be accompanied by cooxidation of xenobiotics resulting in extrahepatic and local tissue production of reactive products which are carcinogenic. The end product prostaglandins, especially prostaglandin E2 (PGE2), are biological modifiers which can significantly affect cell proliferation and tumor growth. High levels of PGE2 stimulate growth of certain tumor cell lines while inhibition of prostaglandin synthesis with indomethacin or piroxicam can cause suppression. The mechanisms for this effect are unclear. Studies in cultured cells exposed to indomethacin show inhibition of G1-to-S phase progression of the cell cycle and a reduction in overall DNA synthesis. It is unclear whether this effect on cell growth results from some direct action of the NSAID or a reduction in prostaglandins or indirectly from modulation of important control signals, such as **calcium flux**. In addition to cyclooxygenase, NSAIDs can inhibit activity of other enzymes, including phosphodiesterases and cyclic GMP-AMP protein kinases, which may be central to cancer initiation and promotion. NSAIDs can also interfere with transmembrane ion fluxes and with cell-to-cell binding. Prostaglandins can modulate a variety of immunological responses and thereby play an important role in host antitumor immunity. For example, high levels of tissue PGE2 are frequently associated with suppression of immune surveillance and killing of malignant cells. Conversely, immune responses are generally enhanced by drugs that inhibit prostaglandin synthesis. PGE2 can act as a feedback inhibitor for cellular immune processes, such as T-cell proliferation, lymphokine production, and cytotoxicity. This effect is also seen for macrophage activity and natural killer cell toxicity. In general, either increased production of PGE2 or increased sensitivity to normal amounts of PGE2 results in depressed cellular immunity. Cyclooxygenase inhibitors (NSAIDs) such as piroxicam which decrease PGE2 production can stimulate cellular immune function both in vitro and in vivo. A variety of tumor cell lines and human malignancies produce large quantities of prostaglandins.(ABSTRACT TRUNCATED AT 400 WORDS)

L14 ANSWER 8 OF 41 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
AN 1997:103010 BIOSIS
DN PREV199799402213
TI Role of Ca-2+ pools in the altered T-cell signalling in rheumatoid arthritis (RA).
AU Carruthers, D. M.; Young, S. P.; Bacon, P. A.
CS Dep. Rheumatol., Univ. Birmingham, Birmingham, UK

SO Immunology, (1996) Vol. 89, No. SUPPL. 1, pp. 75.
Meeting Info.: Joint Congress of the British Society for Immunology and the Biochemical Society. Harrogate, England, UK. December 10-13, 1996.
CODEN: IMMUAM. ISSN: 0019-2805.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
Conference; (Meeting Poster)
LA English
ED Entered STN: 3 Mar 1997
Last Updated on STN: 3 Mar 1997

L14 ANSWER 9 OF 41 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
AN 1994:327662 BIOSIS
DN PREV199497340662
TI Soluble and insoluble immune complexes activate neutrophils using divergent receptor-mediated signal transduction systems.
AU Watson, F.; Robinson, J. J.; Edwards, S. W.
CS Dep. Biochemistry, Univ. Liverpool, P.O. Box 147, Liverpool L69 3BX, UK
SO European Journal of Clinical Investigation, (1994) Vol. 24, No. SUPPL. 2, pp. A29.
Meeting Info.: 28th Annual Scientific Meeting of the European Society for Clinical Investigation. Toledo, Spain. April 20-23, 1994.
CODEN: EJCIB8. ISSN: 0014-2972.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 2 Aug 1994
Last Updated on STN: 3 Aug 1994

L14 ANSWER 10 OF 41 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
AN 1993:255133 BIOSIS
DN PREV199395134308
TI Antinociceptive activity of salmon calcitonin: Electrophysiological correlates in a rat chronic pain model.
AU Braga, P. C. [Reprint author]; Sasso, M. Dal; Bernini, A.; Bartucci, F.; Pollo, A.; Carbone, E.
CS Dip. Farmacologia, Facolta Med., Via Vanvitelli 32, 20129 Milano, Italy
SO Neuroscience Letters, (1993) Vol. 151, No. 1, pp. 85-88.
CODEN: NELED5. ISSN: 0304-3940.
DT Article
LA English
ED Entered STN: 21 May 1993
Last Updated on STN: 22 May 1993
AB Experimental and clinical evidence testifies to an antinociceptive action of salmon calcitonin (sCT), administered in different ways, on the central nervous system. These studies were performed almost exclusively in acute pain models. The purpose of the present study was to investigate the effects of sCT, injected directly into the lateral cerebral ventriculi, on the firing of single nociceptive thalamic neurons, detected by electrophysiological techniques in an experimental model of prolonged or chronic pain, such as rats rendered arthritic by injection of Freund's adjuvant into the left hindfoot. The noxious test stimuli used were either extension or flexion of the ankle or mild lateral pressure on the heel. With increasing doses of sCT (5, 10, 20, 40 mu-g, 5 mu-l/i.c.v.) it was possible to observe correspondingly increasing inhibitory and long-lasting effects on the evoked firing, with a significant dose-effect relationship. In agreement with electrophysiological findings, preliminary data, obtained with a patch clamp technique, on depression of calcium fluxes through neuronal membrane, induced by sCT, oriented the attention to a direct action of sCT on CNS.

L14 ANSWER 11 OF 41 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
AN 93223818 EMBASE
DN 1993223818
TI Bicyclic carboxylic acid LTB4 antagonists.
SO Current Opinion in Therapeutic Patents, (1993) Vol. 3, No. 6, pp. 814-817.

ISSN: 0962-2594 CODEN: COTPES
CY United Kingdom
DT Journal; (Short Survey)
FS 015 Chest Diseases, Thoracic Surgery and Tuberculosis
030 Pharmacology
037 Drug Literature Index
LA English
SL English
ED Entered STN: 930829
Last Updated on STN: 930829
AB Novelty: Novel bicyclic carboxylic acid derivatives are claimed for the treatment of inflammatory diseases such as psoriasis, inflammatory bowel disease, asthma, allergy, **arthritis**, dermatitis, pulmonary disease, ischaemia/reperfusion injury and trauma-induced inflammation. A process for their preparation is also claimed. The compounds are LTB4 antagonists. Biology: In an LTB4 receptor binding assay using human neutrophils the specified compound gave a K(i) value of 1 nM. Inhibition of LTB4-induced **calcium flux** was measured with neutrophils and the compound gave an IC50 value of 2 nM. In an LTB4 induced skin inflamation assay (hairless guinea-pig) the compound gave ID50 values of 10 ng by co-infection with LTB4 and 5 mg/kg by the oral route. The compound inhibited guinea-pig bronchoconstriction in vivo giving ID50 values of 0.01 and 8.70 mg/kg, (iv) and (po) respectively and gave 68% inhibition of acetic acid colitis in rats. Chemistry: The preparation of the compounds is described in thirty-one schemes and exemplified in nearly two-hundred and fifty cases. Six compounds are specifically claimed including 5-(3-carboxypropoxy)-2-[6-[(3,4-dihydro-4-oxo-8-propyl-2H-1-benzopyran-7 -yl)oxy]hexyl]benzene propanoic acid.

L14 ANSWER 12 OF 41 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
AN 93109047 EMBASE
DN 1993109047
TI Piroxicam and other cyclooxygenase inhibitors: Potential for cancer chemoprevention.
AU Earnest D.L.; Hixson L.J.; Alberts D.S.
CS Department of Medicine, Gastroenterology Section, Arizona Health Sciences Center, 1501 N. Campbell Avenue,Tucson, AZ 85724, United States
SO Journal of Cellular Biochemistry, (1992) Vol. 50, No. SUPPL. 16 I, pp. 156-166.
ISSN: 0730-2312 CODEN: JCEBD5
CY United States
DT Journal; Conference Article
FS 016 Cancer
028 Urology and Nephrology
030 Pharmacology
037 Drug Literature Index
LA English
SL English
ED Entered STN: 930516
Last Updated on STN: 930516
AB Piroxicam is a nonsteroidal anti-inflammatory drug (NSAID) widely used for treatment of inflammatory **arthritis**. Recent experimental and clinical studies suggest that piroxicam, as well as other NSAIDs, may be useful for chemoprevention of colon cancer. While there is less information regarding NSAIDs for chemoprevention of urinary bladder malignancy, there are compelling data which suggest that this should be evaluated. A major effect of NSAIDs is inhibition of cyclooxygenase, the rate-limiting enzyme for conversion of arachidonic acid to important signal molecules, including prostaglandins, which profoundly affect cellular functions in many tissues. The initial enzyme reaction leading to formation of prostaglandin H can be accompanied by cooxidation of xenobiotics resulting in extrahepatic and local tissue production of reactive products which are carcinogenic. The end product prostaglandins, especially prostaglandin E2 (PGE2), are biological modifiers which can significantly affect cell proliferation and tumor growth. High levels of PGE2 stimulate growth of certain tumor cell lines while inhibition of prostaglandin synthesis with indomethacin or piroxicam can cause

suppression. The mechanisms for this effect are unclear. Studies in cultured cells exposed to indomethacin show inhibition of G1-to-S phase progression of the cell cycle and a reduction in overall DNA synthesis. It is unclear whether this effect on cell growth results from some direct action of the NSAID or a reduction in prostaglandins or indirectly from modulation of important control signals, such as **calcium flux**. In addition to cyclooxygenase, NSAIDs can inhibit activity of other enzymes, including phosphodiesterases and cyclic GMP-AMP protein kinases, which may be central to cancer initiation and promotion. NSAIDs can also interfere with transmembrane ion fluxes and with cell-to-cell binding. Prostaglandins can modulate a variety of immunological responses and thereby play an important role in host antitumor immunity. For example, high levels of tissue PGE2 are frequently associated with suppression of immune surveillance and killing of malignant cells. Conversely, immune responses are generally enhanced by drugs that inhibit prostaglandin synthesis. PGE2 can act as a feedback inhibitor for cellular immune processes, such as T-cell proliferation, lymphokine production, and cytotoxicity. This effect is also seen for macrophage activity and natural killer cell toxicity. In general, either increased production of PGE2 or increased sensitivity to normal amounts of PGE2 results in depressed cellular immunity. Cyclooxygenase inhibitors (NSAIDs) such as piroxicam which decrease PGE2 production can stimulate cellular immune function both in vitro and in vivo. A variety of tumor cell lines and human malignancies produce large quantities of prostaglandins. Of interest, the concentration of PGE2 is increased in certain premalignant lesions, such as benign adenomatous colon polyps, and further increased in cancerous colon tissue. This observation, taken in context with the effects of prostaglandins on tumor cell growth and immune surveillance, provides strong rationale for study of NSAIDs as potential agents for colon and bladder cancer chemoprevention. During the last decade, more than a dozen animal studies have shown significant protection against development of colon cancer by treatment with NSAIDs piroxicam, indomethacin, and sulindac. Other studies have shown that aspirin protects rats given known carcinogens against colon and bladder cancer. Moreover, patients with familial adenomatous polyposis who are at high risk for colon cancer have, in many instances, experienced regression of colon adenomas during treatment with NSAIDs, particularly sulindac. Most recently, two large epidemiological surveys have reported compelling evidence which suggests the NSAID aspirin may have significant protective activity against colon cancer. This presentation will summarize the rationale for use of piroxicam and other inhibitors of cyclooxygenase as cancer chemoprevention agents and will briefly review results of our approach to evaluating piroxicam as an agent to prevent colon cancer. With this as background, the potential for NSAIDs in chemoprevention against bladder cancer will be explored.

L14 ANSWER 13 OF 41 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 2004:927021 HCAPLUS
DN 141:395421
TI Preparation of cis-2,6-di(pyridyl)piperidines and other cis-di(heteroaryl)-substituted azaheterocycles as binding agents for CXCR4 and other chemokine receptors for treatment of HIV, rheumatoid arthritis, and other diseases and for stimulating progenitor and stem cells
IN Bridger, Gary J.; McEachern, Ernest J.; Skerlj, Renato; Schols, Dominique
PA Anormed Inc., Can.
SO PCT Int. Appl., 221 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004093817	A2	20041104	WO 2004-US12627	20040422
	WO 2004093817	A3	20050428		

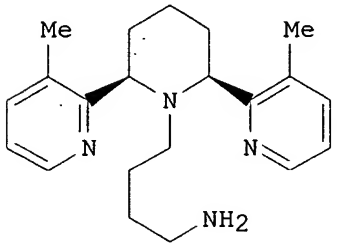
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,

NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,
BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE,
ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI,
SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN,
TD, TG

PRAI US 2003-464858P P 20030422
US 2003-505230P P 20030922

OS MARPAT 141:395421

GI



II

AB Cis-di(heteroaryl)-substituted azaheterocycle compds. A-C(B)-L-Y I [A, B = (un)substituted five- or six-membered heteroaryl moiety containing a nitrogen atom next to the bond to ring C; C = (un)substituted partially or fully saturated azaheterocycle with 5-8 ring atoms; L = (un)substituted alkanediyl, alkenediyl, alkynediyl; Y = H, (un)substituted alkyl which may contain heteroatoms, (un)substituted cyclic group; at least one of A or B must be substituted when C is either a piperidinyl or 1,2,3,6-tetrahydropyridinyl ring, and both A and B may not be substituted with naphthalenyl groups if A and B are pyridinyl groups and if C is a piperidinyl moiety; if L-Y is Me, C is not 4-oxo-3,5-piperidinedicarboxylic acid, and if L-Y is benzyl, C is not a 4-hydroxy-1,2,5,6-tetrahydro-3-pyridinecarboxylic acid ester] such as II are prepared as agents capable of binding to chemokine receptors (particularly the CXCR4 receptor) for treatment of a variety of conditions such as HIV infection, cancer, inflammation, rheumatoid **arthritis**, immune system disorders, or diseases requiring stimulation of progenitor or stem cells for treatment. Lithium-bromine exchange of 2-bromo-3-methylpyridine followed by addition of the pyridyllithium to di-Me glutarate yields 1,5-bis(3-methyl-2-pyridinyl)-1,5-pentanedione; reduction of the dione with sodium borohydride in methanol to the dipyridinylpentanediol, dimesylation, substitution and cyclization with allylamine and separation of the cis- and trans-piperidines, palladium-mediated N-deallylation, alkylation of the piperidine nitrogen with 4-(N-phthalimidyl)-1-bromobutane, and hydrazine-mediated cleavage of the phthalimide yields II. Compds. I inhibit HIV replication with IC50 values between 0.5 nM and 5 μM, and inhibit SDF-1α-induced **calcium flux** with IC50 values between 0.5 nM and 5 μM (no data). Compds. of the invention increase and mobilize mouse and human progenitor cells, increase white blood cell count in HIV-infected people, and mobilize CD34-pos. cells in humans; in addition, compds. of the invention mobilize bone marrow cells to repair heart muscle (no data).

L14 ANSWER 14 OF 41 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 2004:550936 HCAPLUS
DN 141:89119
TI A preparation of (piperidinyl-N-carboxy)pyrimidine derivatives, useful as CCR5 antagonists
IN Miller, Michael W.; Scott, Jack D.
PA Schering Corporation, USA
SO PCT Int. Appl., 50 pp.
CODEN: PIXXD2
DT Patent
LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004056770	A2	20040708	WO 2003-US40619	20031217
	WO 2004056770	A3	20040812		

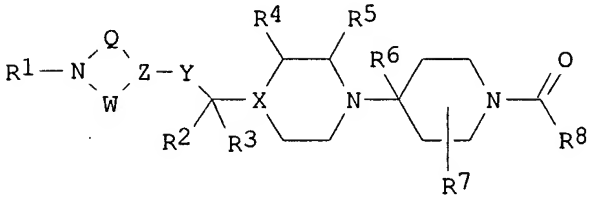
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LU, LV, MA, MD, MG, MK, MN, MX, MZ, NI, NO, NZ, PG, PH, PL, PT, RO, RU, SC, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UZ, VC, VN, YU, ZA, ZM

RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

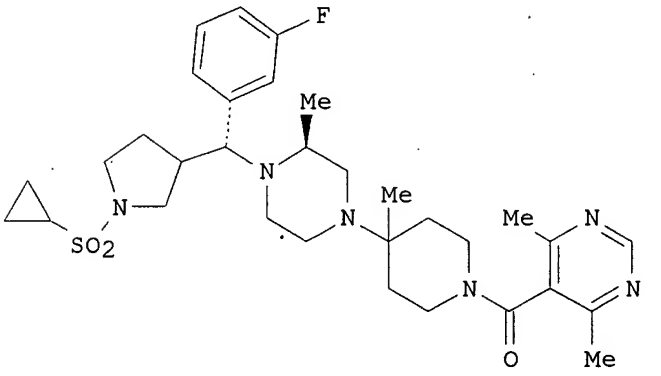
	US 2004132711	A1	20040708	US 2003-738907	20031217
PRAI	US 2002-434306P	P	20021218		

OS MARPAT 141:89119

GI



I



II

AB The invention relates to a preparation of (piperidinyl-N-carboxy)pyrimidine derivs. of formula I [wherein: X and Z are independently selected from N or CH; R1 = H, alkyl, arylalkyl, SO2-alkyl, C(O)-alkyl, or C(O)-aryl, etc.; R2, R4, R5, R6, and R7 are independently represent H or alkyl; R3 is H, (cyclo)alkyl, or (hetero)aryl, etc.; R8 is (hetero)aryl, fluorenyl, or pyrimidinyl, etc.; Y and W are independently selected from (CH2)0-4; Q is (CH2)1-4], useful as CCR5 antagonists. The invention also relates to the use of a combination of compds. of this invention and one or more antiviral or other agents useful in the treatment of Human Immunodeficiency Virus (HIV). The invention further relates to the use of compds. of this invention, alone or in combination with another agent, in the treatment of solid organ transplant rejection, graft v. host disease, **arthritis**, rheumatoid **arthritis**, inflammatory bowel disease, atopic dermatitis, psoriasis, asthma, allergies or multiple sclerosis. The obtained title compds. were screened in HIV-1 entry assay, HIV-1 replication assay, **calcium flux** assay, GTPγS binding assay, luciferase replication assay, and chemotaxis assay, etc. For instance, IC50 for (piperidinyl-N-carboxy)pyrimidine derivative II was found as 0.3 nM (luciferase replication assay).

L14 ANSWER 15 OF 41 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 2002:669612 HCAPLUS
DN 137:212635
TI Human vanilloid receptor-2 protein and its encoding nucleic acid sequence and role in mediation of intracellular calcium flux in response to external stimuli
IN Young, Paul E.; Ruben, Steven M.
PA Human Genome Sciences, Inc., USA
SO U.S., 78 pp., Cont.-in-part of Appl. No. PCT/US98/04493.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 43

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6444440	B1	20020903	US 1998-132316	19980811
	CA 2283299	AA	19980911	CA 1998-2283299	19980306
	CA 2284131	AA	19980911	CA 1998-2284131	19980306
	WO 9839448	A2	19980911	WO 1998-US4493	19980306
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	EP 1352962	A1	20031015	EP 2003-6291	19980306
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	EP 1394252	A2	20040303	EP 2003-9752	19980306
	EP 1394252	A3	20040310		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	US 2002164669	A1	20021107	US 2001-981876	20011019
	US 2003022289	A1	20030130	US 2002-137316	20020503
	US 6906178	B2	20050614		
PRAI	US 1997-40163P	P	19970307		
	WO 1998-US4493	A2	19980306		
	US 1997-38621P	P	19970307		
	US 1997-40161P	P	19970307		
	US 1997-40162P	P	19970307		
	US 1997-40333P	P	19970307		
	US 1997-40334P	P	19970307		
	US 1997-40336P	P	19970307		
	US 1997-40626P	P	19970307		
	US 1997-43311P	P	19970411		
	US 1997-43312P	P	19970411		
	US 1997-43313P	P	19970411		
	US 1997-43314P	P	19970411		
	US 1997-43315P	P	19970411		
	US 1997-43568P	P	19970411		
	US 1997-43569P	P	19970411		
	US 1997-43576P	P	19970411		
	US 1997-43578P	P	19970411		
	US 1997-43580P	P	19970411		
	US 1997-43669P	P	19970411		
	US 1997-43670P	P	19970411		
	US 1997-43671P	P	19970411		
	US 1997-43672P	P	19970411		
	US 1997-43674P	P	19970411		
	US 1997-47492P	P	19970523		
	US 1997-47500P	P	19970523		
	US 1997-47502P	P	19970523		
	US 1997-47503P	P	19970523		
	US 1997-47581P	P	19970523		
	US 1997-47582P	P	19970523		
	US 1997-47583P	P	19970523		

US 1997-47584P P 19970523
US 1997-47587P P 19970523
US 1997-47592P P 19970523
US 1997-47596P P 19970523
US 1997-47597P P 19970523
US 1997-47598P P 19970523
US 1997-47600P P 19970523
US 1997-47601P P 19970523
US 1997-47612P P 19970523
US 1997-47613P P 19970523
US 1997-47615P P 19970523
US 1997-47617P P 19970523
US 1997-47618P P 19970523
US 1997-47632P P 19970523
US 1997-47633P P 19970523
US 1997-61060P P 19971002
EP 1998-905126 A3 19980306
US 1998-132316 A3 19980811
EP 1998-905127 A3 19980911
US 2000-621011 A3 20000720

AB The present invention relates to vanilloid receptor-2 (VR2), a novel member of the vanilloid receptor family. The invention provides the isolated cDNA mols. encoding human VR2 receptors. The VR2 polypeptide contains 4 intracellular and 4 extracellular domains, 6 transmembrane domains with a pore loop between transmembrane domains 5 and 6, and 3 ankyrin repeat motifs in the N-terminal hydrophilic domain. Northern anal. reveals expression of the VR2 transcript in a variety of tissues, with highest levels in the spleen, lymph node, peripheral blood leukocytes , and lung; next highest levels of expression were observed in the thymus, heart, placenta, brain, bone marrow, and fetal liver; and lower expression in other tissues. VR2 polypeptides are also provided, as are vectors, host cells and recombinant methods for producing the same. The invention further relates to screening methods for identifying agonists and antagonists of VR2 receptor activity. Also provided are diagnostic methods for detecting disease states related to the aberrant expression of VR2 receptors. Further provided are therapeutic methods for treating disease states including, but not limited to, chronic pain syndromes, congenital pain insensitivity, inflammation, ischemia, host defense dysfunction, immune surveillance dysfunction, arthritis, multiple sclerosis, autoimmunity, immune dysfunction, and allergy.

RE.CNT 78 THERE ARE 78 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 16 OF 41 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 2001:396700 HCAPLUS
DN 135:32749
TI "Bonzo" chemokine receptor antibodies and ligands
IN Briskin, Michael J.; Murphy, Kristine E.; Wilbanks, Alyson M.; Wu, Lijun
PA Millennium Pharmaceuticals, Inc., USA
SO PCT Int. Appl., 190 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001037872	A1	20010531	WO 2000-US32206	20001122
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6319675	B1	20011120	US 1999-449437	19991124
EP 1233785	A1	20020828	EP 2000-980738	20001122

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

	US 2002090657	A1	20020711	US 2001-940063	20010827
	US 2003165995	A1	20030904	US 2002-174293	20020617
PRAI	US 1999-449437	A	19991124		
	US 2000-722064	B1	20001122		
	WO 2000-US32206	W	20001122		

AB The invention relates to an antibody or antigen-binding fragment thereof which binds to the CXC chemokine receptor Bonzo (also referred to as STRL33, TYMSTR, HBMBU14 and CXCR6) and blocks the binding of a ligand e.g., SExCkine (also referred to as chemokine alpha-5 and CXCL16) to the receptor. The invention also relates to a method of identifying agents (mols., compds.) which can bind to Bonzo and inhibit the binding of a ligand (e.g. SExCkine) and/or modulate a function of Bonzo. The invention relates to an antibody or antigen-binding fragment thereof which binds to the CXC chemokine SExCkine and inhibits binding of SExCkine to Bonzo receptor. The invention also relates to targeting mols. which contain a first binding moiety which binds to mammalian Bonzo and a second binding moiety which binds to a mol. expressed on the surface of a target cell. The invention also relates to a method of promoting and/or effectuating the interaction of a Bonzo+ cell and a target cell. The invention further relates to a method of modulating a function of Bonzo, and to the use of the antibodies, antigen-binding fragments, targeting mols. and agents identified by the method of the invention in research, therapeutic, prophylactic and diagnostic methods.

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 17 OF 41 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 1996:509833 HCAPLUS
DN 125:193223
TI Characterization of altered calcium signalling in T lymphocytes from patients with rheumatoid arthritis (RA)
AU Carruthers, D. M.; Naylor, W. G.; Allen, M. E.; Kitas, G. D.; Bacon, P. A.; Young, S. P.
CS Department of Rheumatology, University of Birmingham, Birmingham, UK
SO Clinical and Experimental Immunology (1996), 105(2), 291-296
CODEN: CEXIAL; ISSN: 0009-9104
PB Blackwell
DT Journal
LA English
AB Abnormal function of peripheral blood T lymphocytes is characteristic of RA; diminished proliferation and secretion of cytokines following in vitro mitogen stimulation are observed We have investigated the calcium flux initiating T cell activation in rheumatoid peripheral blood mononuclear cells (PBMC) to determine whether abnormalities in signalling are also present. We have found that both phytohemagglutinin (PHA-P)- and anti-CD3-stimulated calcium fluxes were much reduced in the patients' PBMC compared with controls, with a mean six-fold difference ($P < 0.01$) in rate of Ca2+ flux with PHA-P stimulation. When purified T cells were examined with PHA and CD3 stimulation, a reduction in the peak and plateau [Ca2+]i was observed in RA T cells, but the rate of rise of [Ca2+]i was only reduced in those cells stimulated with PHA. These results suggest that alterations in the initiating signal may underlie the functional T cell abnormalities associated with RA, and that there may be an addnl. extrinsic influence from non-T cells in the PBMC population.

L14 ANSWER 18 OF 41 USPATFULL on STN
AN 2005:144237 USPATFULL
TI Chimeric chemokine receptor polypeptides
IN Dinchuk, Joseph E., Stockton, NJ, UNITED STATES
Davies, Paul, Wilmington, DE, UNITED STATES
Zhao, Qihong, Princeton, NJ, UNITED STATES
Carter, Percy H., Princeton, NJ, UNITED STATES
Solomon, Kimberly A., Landenberg, PA, UNITED STATES
Scherle, Peggy Ann, Media, PA, UNITED STATES

PI	US 2005123972	A1	20050609		
AI	US 2004-988267	A1	20041112 (10)		

PRAI US 2003-519605P 20031113 (60)
DT Utility
FS APPLICATION
LREP STEPHEN B. DAVIS, BRISTOL-MYERS SQUIBB COMPANY, PATENT DEPARTMENT, P O BOX 4000, PRINCETON, NJ, 08543-4000, US
CLMN Number of Claims: 39
ECL Exemplary Claim: 1
DRWN 11 Drawing Page(s)
LN.CNT 3132
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to a chimeric chemokine receptor comprising two components: a first sequence comprising the N terminus through the last residue of the seven helix TM region of a first chemokine receptor joined with a second sequence comprising the C terminus of a second chemokine receptor extending from the first intracellular residue of the chemokine receptor to the last residue of the chemokine receptor. The chimeric chemokine receptor can be employed in various applications, such as ligand binding and screening assays and signalling assays. The chimeric chemokine receptor can also form a component of a chemokine receptor modulator design program.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L14 ANSWER 19 OF 41 USPATFULL on STN
AN 2005:68497 USPATFULL
TI Use of effectors of glutaminyl and glutamate cyclases
IN Demuth, Hans-Ulrich, Halle/Saale, GERMANY, FEDERAL REPUBLIC OF
Hoffmann, Torsten, Halle/Saale, GERMANY, FEDERAL REPUBLIC OF
Niestroj, Andre J., Sennewltz, GERMANY, FEDERAL REPUBLIC OF
Schilling, Stephan, Halle/Saale, GERMANY, FEDERAL REPUBLIC OF
Heiser, Ulrich, Halle/Saale, GERMANY, FEDERAL REPUBLIC OF
PI US 2005058635 A1 20050317
AI US 2004-839017 A1 20040505 (10)
PRAI US 2003-468043P 20030505 (60)
US 2003-512038P 20031015 (60)
US 2003-468014P 20030505 (60)
DT Utility
FS APPLICATION
LREP BROWN, RUDNICK, BERLACK & ISRAELS, LLP., BOX IP, 18TH FLOOR, ONE FINANCIAL CENTER, BOSTON, MA, 02111
CLMN Number of Claims: 47
ECL Exemplary Claim: 1
DRWN 21 Drawing Page(s)
LN.CNT 3120
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention provides novel physiological substrates of mammalian glutaminyl cyclase (QC, EC 2.3.2.5), new effectors of QC, methods for screeing for such effectors, and the use of such effectors and pharmaceutical compositions comprising such effectors for the treatment of conditions that can be treated by modulation of QC-activity. Preferred compositions additionally comprise inhibitors of DP IV or DP IV-like enzymes for the treatment or alleviation of conditions that can be treated by modulation of QC- and DP IV-activity.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L14 ANSWER 20 OF 41 USPATFULL on STN
AN 2004:286707 USPATFULL
TI Inhibitors of glutaminyl cyclase
IN Schilling, Stephan, Halle/Saale, GERMANY, FEDERAL REPUBLIC OF
Niestroj, Andre J., Sennewitz, GERMANY, FEDERAL REPUBLIC OF
Heiser, Ulrich, Halle/Saale, GERMANY, FEDERAL REPUBLIC OF
Buchholz, Mirko, Halle/Saale, GERMANY, FEDERAL REPUBLIC OF
Demuth, Hans-Ulrich, Halle/Saale, GERMANY, FEDERAL REPUBLIC OF
PI US 2004224875 A1 20041111
AI US 2004-838993 A1 20040505 (10)
PRAI US 2003-468014P 20030505 (60)
DT Utility

FS APPLICATION
LREP BROWN, RUDNICK, BERLACK & ISRAELS, LLP., BOX IP, 18TH FLOOR, ONE FINANCIAL CENTER, BOSTON, MA, 02111
CLMN Number of Claims: 34
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 2301
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to compounds that act as inhibitors of QC including those represented by the general formulae 1 to 9: ##STR1##

and combinations thereof for the treatment of neuronal disorders, especially Alzheimer's disease, Down Syndrome, Parkinson disease, Corea Huntington, pathogenic psychotic conditions, schizophrenia, impaired food intake, sleep-wakefulness, impaired homeostatic regulation of energy metabolism, impaired autonomic function, impaired hormonal balance, impaired regulation, body fluids, hypertension, fever, sleep dysregulation, anorexia, anxiety related disorders including depression, seizures including epilepsy, drug withdrawal and alcoholism, neurodegenerative disorders including cognitive dysfunction and dementia.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L14 ANSWER 21 OF 41 USPATFULL on STN
AN 2004:189733 USPATFULL
TI T1 receptor-like ligand II
IN Ni, Jian, Germantown, MD, UNITED STATES
Gentz, Reiner L., Belo Horizonte-Mg, BRAZIL
Ruben, Steven M., Brookeville, MD, UNITED STATES
PA Human Genome Sciences, Inc., Rockville, MD, UNITED STATES, 20850 (U.S. corporation)
PI US 2004146501 A1 20040729
AI US 2003-692730 A1 20031027 (10)
RLI Division of Ser. No. US 1999-317641, filed on 25 May 1999, GRANTED, Pat. No. US 6667032 Division of Ser. No. US 1997-916442, filed on 22 Aug 1997, GRANTED, Pat. No. US 6586210
PRAI US 1996-24348P 19960823 (60)
DT Utility
FS APPLICATION
LREP HUMAN GENOME SCIENCES INC, INTELLECTUAL PROPERTY DEPT., 14200 SHADY GROVE ROAD, ROCKVILLE, MD, 20850
CLMN Number of Claims: 90
ECL Exemplary Claim: 1
DRWN 4 Drawing Page(s)
LN.CNT 2937
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention concerns a novel T1R-like ligand II protein. In particular, isolated nucleic acid molecules are provided encoding the T1R-like ligand II protein. T1R-like ligand II polypeptides are also provided, as are recombinant vectors and host cells for expressing the same.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L14 ANSWER 22 OF 41 USPATFULL on STN
AN 2004:179273 USPATFULL
TI T1-R ligand III
IN Ni, Jian, Germantown, MD, UNITED STATES
Gentz, Reiner L., Belo Horizonte-Mg, BRAZIL
Ruben, Steven M., Brookeville, MD, UNITED STATES
PA Human Genome Sciences, Inc., Rockville, MD, UNITED STATES (U.S. corporation)
PI US 2004138443 A1 20040715
AI US 2004-775165 A1 20040211 (10)
RLI Continuation of Ser. No. US 2002-215088, filed on 9 Aug 2002, PENDING Continuation of Ser. No. US 1998-30847, filed on 26 Feb 1998, ABANDONED
PRAI US 1997-39483P 19970228 (60)

DT Utility
FS APPLICATION
LREP HUMAN GENOME SCIENCES INC, INTELLECTUAL PROPERTY DEPT., 14200 SHADY GROVE ROAD, ROCKVILLE, MD, 20850
CLMN Number of Claims: 24
ECL Exemplary Claim: 1
DRWN .9 Drawing Page(s)
LN.CNT 3074
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to a novel T1-R ligand III protein which is a member of the IL-1RI ligand-like family. In particular, isolated nucleic acid molecules are provided encoding the human T1-R ligand III protein. T1-R ligand III polypeptides are also provided as are vectors, host cells and recombinant methods for producing the same. The invention further relates to screening methods for identifying agonists and antagonists of T1-R ligand III activity. Also provided are diagnostic methods for detecting immune system-related disorders and therapeutic methods for treating immune system-related disorders.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L14 ANSWER 23 OF 41 USPATFULL on STN
AN 2004:173188 USPATFULL
TI Identification, monitoring and treatment of disease and characterization of biological condition using gene expression profiles
IN Bevilacqua, Michael, Boulder, CO, UNITED STATES
Cheronis, John C., Conifer, CO, UNITED STATES
Tryon, Victor, Loveland, CO, UNITED STATES
PI US 2004133352 A1 20040708
AI US 2002-291225 A1 20021108 (10)
RLI Continuation-in-part of Ser. No. US 2001-821850, filed on 29 Mar 2001, GRANTED, Pat. No. US 6692916 Continuation-in-part of Ser. No. US 2000-605581, filed on 28 Jun 2000, ABANDONED
PRAI US 2001-348213P 20011109 (60)
US 2001-340881P 20011207 (60)
US 2002-369633P 20020403 (60)
US 2002-376997P 20020430 (60)
US 1999-141542P 19990628 (60)
US 2000-195522P 20000407 (60)
DT Utility
FS APPLICATION
LREP BROMBERG & SUNSTEIN LLP, 125 SUMMER STREET, BOSTON, MA, 02110-1618
CLMN Number of Claims: 77
ECL Exemplary Claim: 1
DRWN 44 Drawing Page(s)
LN.CNT 4839
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Gene expression data, in particular gene expression profiles, are created and used in the identification, monitoring and treatment of disease and characterization of biological conditions. Profile data sets are derived from subject samples and include quantitative substantially repeatable measures of a distinct amount of RNA or protein constituent in a panel selected to enable evaluation of a biological condition. Such profile data sets may be used to provide an index indicative of the biological state of a subject, which may be compared to a normative value of the index determined with respect to a relevant population of subjects.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L14 ANSWER 24 OF 41 USPATFULL on STN
AN 2004:164883 USPATFULL
TI Method of alleviating chronic pain via peripheral inhibition of neurotransmitter synthesis
IN Miller, Kenneth E., Sapulpa, OK, UNITED STATES
PI US 2004126368 A1 20040701
AI US 2003-660093 A1 20030911 (10)
RLI Continuation-in-part of Ser. No. US 2002-245098, filed on 13 Sep 2002,

PENDING
PRAI US 2002-411311P 20020913 (60)
US 2001-318861P 20010913 (60)
DT Utility
FS APPLICATION
LREP DUNLAP, CODDING & ROGERS P.C., PO BOX 16370, OKLAHOMA CITY, OK, 73113
CLMN Number of Claims: 23
ECL Exemplary Claim: 1
DRWN 30 Drawing Page(s)
LN.CNT 2697
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A composition having sustained pain-relieving properties such that the composition may be administered to a subject to alleviate chronic pain. The composition includes an effective amount of at least one inhibitor of neurotransmitter synthesis. A method for alleviating chronic pain in a subject for an extended period of time is also disclosed, in which the compound is administered to a subject suffering from chronic pain at a site of inflammation such that the administration of the compound results in a reduction in at least one of thermal and mechanical pain responses at the site of inflammation for a period of at least two days without any resulting acute pain behavior. The composition may further include an effective amount of at least one compound having analgesic effects such that the composition also alleviates acute pain.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L14 ANSWER 25 OF 41 USPATFULL on STN
AN 2004:64346 USPATFULL
TI Antagonists of chemokine receptors
IN Purandare, Ashok V., Pennington, NJ, UNITED STATES
PI US 2004048865 A1 20040311
AI US 2003-648677 A1 20030825 (10)
PRAI US 2002-406219P 20020827 (60)
DT Utility
FS APPLICATION
LREP STEPHEN B. DAVIS, BRISTOL-MYERS SQUIBB COMPANY, PATENT DEPARTMENT, P O BOX 4000, PRINCETON, NJ, 08543-4000
CLMN Number of Claims: 12
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1422
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Compounds are provided which are antagonists of chemokine receptor activity.

The compounds thereof have the structure ##STR1##

including enantiomers, diastereomers, tautomers, pharmaceutically acceptable salts and solvates thereof wherein:

A, B, D, E, X and Y are selected from N or C, J and K are C, and at least one of A, B, D, E, X and Y is N;

L is selected from O, NH and S, wherein L may be connected to any one of A, B, D, E, J, X, K or Y;

M is CH or N;

P is a bond or C.dbd.O, wherein P is connected to any one of J, X, K or Y;

Z is --(CFG)R.sup.2 where F is O, H.sub.2, alkyl or substituted alkyl and G is O or N or none;

n is 0-4;

R.sup.1 is selected from halogen, --CN, --CF.sub.3, substituted alkyl, aryl and heteroaryl;

R.sup.2 is a heterocyclyl containing at least one N;

R.sup.3 is selected from halogen, cyano, alkyl, substituted alkyl, aryl, substituted aryl, heteroaryl and substituted heteroaryl, wherein R.sup.3 is connected to any one of A, B, D and E;

R.sup.4 and R.sup.5 are H;

or R.sup.4 and R.sup.5 may be taken together with the atoms to which they are attached to form a ring; and

R.sup.10 is selected from H, alkyl, substituted alkyl, alkenyl, substituted alkenyl;

or E and R.sup.10 may be taken together with the atoms to which they are attached to form a heteroaryl or heterocycloalkyl ring.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L14 ANSWER 26 OF 41 USPATFULL on STN
AN 2004:58184 USPATFULL
TI 123 human secreted proteins
IN Fischer, Carrie L., Burke, VA, UNITED STATES
Rosen, Craig A., Laytonsville, MD, UNITED STATES
Soppet, Daniel R., Centreville, VA, UNITED STATES
Ruben, Steven M., Olney, MD, UNITED STATES
Kyaw, Hla, Frederick, MD, UNITED STATES
Li, Yi, Sunnyvale, CA, UNITED STATES
Zeng, Zhizhen, Lansdale, PA, UNITED STATES
LaFleur, David W., Washington, DC, UNITED STATES
Moore, Paul A., Germantown, MD, UNITED STATES
Shi, Yanggu, Gaithersburg, MD, UNITED STATES
Olsen, Henrik, Gaithersburg, MD, UNITED STATES
Ebner, Reinhard, Gaithersburg, MD, UNITED STATES
Birse, Charles E., North Potomac, MD, UNITED STATES
PI US 2004044191 A1 20040304
AI US 2001-973278 A1 20011010 (9)
RLI Continuation-in-part of Ser. No. US 1999-227357, filed on 8 Jan 1999, GRANTED, Pat. No. US 6342581 Continuation-in-part of Ser. No. WO 1998-US13684, filed on 7 Jul 1998, UNKNOWN
PRAI US 2000-239899P 20001013 (60)
US 1997-51926P 19970708 (60)
US 1997-52793P 19970708 (60)
US 1997-51925P 19970708 (60)
US 1997-51929P 19970708 (60)
US 1997-52803P 19970708 (60)
US 1997-52732P 19970708 (60)
US 1997-51931P 19970708 (60)
US 1997-51932P 19970708 (60)
US 1997-51916P 19970708 (60)
US 1997-51930P 19970708 (60)
US 1997-51918P 19970708 (60)
US 1997-51920P 19970708 (60)
US 1997-52733P 19970708 (60)
US 1997-52795P 19970708 (60)
US 1997-51919P 19970708 (60)
US 1997-51928P 19970708 (60)
US 1997-55722P 19970818 (60)
US 1997-55723P 19970818 (60)
US 1997-55948P 19970818 (60)
US 1997-55949P 19970818 (60)
US 1997-55953P 19970818 (60)
US 1997-55950P 19970818 (60)
US 1997-55947P 19970818 (60)
US 1997-55964P 19970818 (60)
US 1997-56360P 19970818 (60)
US 1997-55684P 19970818 (60)

US 1997-55984P 19970818 (60)
US 1997-55954P 19970818 (60)
US 1997-58785P 19970912 (60)
US 1997-58664P 19970912 (60)
US 1997-58660P 19970912 (60)
US 1997-58661P 19970912 (60)
DT Utility
FS APPLICATION
LREP HUMAN GENOME SCIENCES INC, 9410 KEY WEST AVENUE, ROCKVILLE, MD, 20850
CLMN Number of Claims: 24
ECL Exemplary Claim: 1
DRWN 3 Drawing Page(s)
LN.CNT 36492
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to novel human secreted proteins and isolated nucleic acids containing the coding regions of the genes encoding such proteins. Also provided are vectors, host cells, antibodies, and recombinant methods for producing human secreted proteins. The invention further relates to diagnostic and therapeutic methods useful for diagnosing and treating diseases, disorders, and/or conditions related to these novel human secreted proteins.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L14 ANSWER 27 OF 41 USPATFULL on STN
AN 2004:50848 USPATFULL
TI 125 human secreted proteins
IN Rosen, Craig A., Laytonsville, MD, UNITED STATES
Feng, Ping, Germantown, MD, UNITED STATES
Ruben, Steven M., Brookeville, MD, UNITED STATES
Ebner, Reinhard, Gaithersburg, MD, UNITED STATES
Olsen, Henrik, Gaithersburg, MD, UNITED STATES
Ni, Jian, Germantown, MD, UNITED STATES
Wei, Ying-Fei, Berkeley, CA, UNITED STATES
Soppet, Daniel R., Centreville, VA, UNITED STATES
Moore, Paul A., Germantown, MD, UNITED STATES
Kyaw, Hla, Boonsboro, MD, UNITED STATES
LaFleur, David W., Washington, DC, UNITED STATES
Shi, Yanggu, Gaithersburg, MD, UNITED STATES
Janat, Fouad, Westerly, RI, UNITED STATES
Endress, Gregory A., Florence, MA, UNITED STATES
Carter, Kenneth C., North Potomac, MD, UNITED STATES
Birse, Charles E., North Potomac, MD, UNITED STATES
PA Human Genome Sciences, Inc., Rockville, MD, UNITED STATES, 20850 (U.S. corporation)
PI US 2004038277 A1 20040226
AI US 2003-621401 A1 20030718 (10)
RLI Continuation of Ser. No. US 2001-974879, filed on 12 Oct 2001, PENDING Continuation-in-part of Ser. No. US 2001-818683, filed on 28 Mar 2001, PENDING Continuation of Ser. No. US 1999-305736, filed on 5 May 1999, PENDING Continuation-in-part of Ser. No. WO 1998-US23435, filed on 4 Nov 1998, PENDING
PRAI US 2000-239893P 20001013 (60)
US 1997-64911P 19971107 (60)
US 1997-64912P 19971107 (60)
US 1997-64983P 19971107 (60)
US 1997-64900P 19971107 (60)
US 1997-64988P 19971107 (60)
US 1997-64987P 19971107 (60)
US 1997-64908P 19971107 (60)
US 1997-64984P 19971107 (60)
US 1997-64985P 19971107 (60)
US 1997-66094P 19971117 (60)
US 1997-66100P 19971117 (60)
US 1997-66089P 19971117 (60)
US 1997-66095P 19971117 (60)
US 1997-66090P 19971117 (60)
DT Utility

FS APPLICATION
LREP HUMAN GENOME SCIENCES INC, 9410 KEY WEST AVENUE, ROCKVILLE, MD, 20850
CLMN Number of Claims: 23
ECL Exemplary Claim: 1
DRWN 3 Drawing Page(s)
LN.CNT 38927
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to novel human secreted proteins and isolated nucleic acids containing the coding regions of the genes encoding such proteins. Also provided are vectors, host cells, antibodies, and recombinant methods for producing human secreted proteins. The invention further relates to diagnostic and therapeutic methods useful for diagnosing and treating diseases, disorders, and/or conditions related to these novel human secreted proteins.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L14 ANSWER 28 OF 41 USPATFULL on STN
AN 2003:312174 USPATFULL
TI Identification, monitoring and treatment of disease and characterization of biological condition using gene expression profiles
IN Bevilacqua, Michael, Boulder, CO, UNITED STATES
Cheronis, John C., Conifer, CO, UNITED STATES
Tryon, Victor, Loveland, CO, UNITED STATES
PI US 2003219771 A1 20031127
AI US 2002-291856 A1 20021108 (10)
PRAI US 2001-348213P 20011109 (60)
US 2001-340881P 20011207 (60)
US 2002-369633P 20020403 (60)
US 2002-376997P 20020430 (60)
DT Utility
FS APPLICATION
LREP BROMBERG & SUNSTEIN LLP, 125 SUMMER STREET, BOSTON, MA, 02110-1618
CLMN Number of Claims: 77
ECL Exemplary Claim: 1
DRWN 44 Drawing Page(s)
LN.CNT 4844
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Gene expression data, in particular gene expression profiles, are created and used in the identification, monitoring and treatment of disease and characterization of biological conditions. Profile data sets are derived from subject samples and include quantitative substantially repeatable measures of a distinct amount of RNA or protein constituent in a panel selected to enable evaluation of a biological condition. Such profile data sets may be used to provide an index indicative of the biological state of a subject, which may be compared to a normative value of the index determined with respect to a relevant population of subjects.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L14 ANSWER 29 OF 41 USPATFULL on STN
AN 2003:302869 USPATFULL
TI Tetrahydroisoquinoline analogs as modulators of chemokine receptor activity
IN Hermsmeier, Mark Alden, Somerville, NJ, United States
Rawlins, David B., Morrisville, PA, United States
Wityak, John, Robbinsville, NJ, United States
PA Bristol-Myers Squibb Co., Princeton, NJ, United States (U.S. corporation)
PI US 6649606 B1 20031118
AI US 2002-289671 20021107 (10)
PRAI US 2001-346377P 20011109 (60)
DT Utility
FS GRANTED
EXNAM Primary Examiner: Davis, Zinna Northington
LREP Duncan, Laurelee A.
CLMN Number of Claims: 12

ECL Exemplary Claim: 1
DRWN 0 Drawing Figure(s); 0 Drawing Page(s)
LN.CNT 1935
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Tetrahydroisoquinoline analogs are provided which are modulators of chemokine receptor activity.

The tetrahdroisoquinoline analogs thereof have the structure ##STR1##

wherein R.sub.1, R.sub.2, R.sub.3, R.sub.3a, X.sub.1, X.sub.2, X.sub.3, X.sub.4, m, n and p are as described herein.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L14 ANSWER 30 OF 41 USPATFULL on STN
AN 2003:300249 USPATFULL
TI 125 human secreted proteins
IN Feng, Ping, Gaithersburg, MD, UNITED STATES
Ruben, Steven M., Olney, MD, UNITED STATES
Rosen, Craig A., Laytonsville, MD, UNITED STATES
Ebner, Reinhard, Gaithersburg, MD, UNITED STATES
Olsen, Henrik S., Gaithersburg, MD, UNITED STATES
Ni, Jian, Rockville, MD, UNITED STATES
Wei, Ying-Fei, Berkeley, CA, UNITED STATES
Soppet, Daniel R., Centreville, VA, UNITED STATES
Moore, Paul A., Germantown, MD, UNITED STATES
Kyaw, Hla, Frederick, MD, UNITED STATES
LaFleur, David W., Washington, DC, UNITED STATES
Shi, Yanggu, Gaithersburg, MD, UNITED STATES
Janat, Fouad, Westerly, RI, UNITED STATES
Endress, Gregory A., Potomac, MD, UNITED STATES
Carter, Kenneth C., North Potomac, MD, UNITED STATES
PI US 2003211472 A1 20031113
US 2004185440 A9 20040923
AI US 2001-818683 A1 20010328 (9)
RLI Continuation of Ser. No. US 1999-305736, filed on 5 May 1999, UNKNOWN
DT Utility
FS APPLICATION
LREP HUMAN GENOME SCIENCES INC, 9410 KEY WEST AVENUE, ROCKVILLE, MD, 20850
CLMN Number of Claims: 23
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 22344
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to novel human secreted proteins and isolated nucleic acids containing the coding regions of the genes encoding such proteins. Also provided are vectors, host cells, antibodies, and recombinant methods for producing human secreted proteins. The invention further relates to diagnostic and therapeutic methods useful for diagnosing and treating disorders related to these novel human secreted proteins.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L14 ANSWER 31 OF 41 USPATFULL on STN
AN 2003:282277 USPATFULL
TI T1 receptor-like ligand II and uses thereof
IN Ni, Jian, Germantown, MD, UNITED STATES
Gentz, Reiner L., Belo Horizonte-Mg, BRAZIL
Ruben, Steven M., Brookeville, MD, UNITED STATES
PA Human Genome Sciences, Inc., Rockville, MD (U.S. corporation)
PI US 2003198618 A1 20031023
AI US 2003-439222 A1 20030516 (10)
RLI Division of Ser. No. US 2000-731924, filed on 8 Dec 2000, GRANTED, Pat. No. US 6605271 Continuation-in-part of Ser. No. US 1999-317641, filed on 25 May 1999, PENDING Division of Ser. No. US 1997-916442, filed on 22 Aug 1997, GRANTED, Pat. No. US 6586210
PRAI US 1996-24348P 19960823 (60)

US 1999-169979P 19991210 (60)
DT Utility
FS APPLICATION
LREP HUMAN GENOME SCIENCES INC, 9410 KEY WEST AVENUE, ROCKVILLE, MD, 20850
CLMN Number of Claims: 11
ECL Exemplary Claim: 1
DRWN 5 Drawing Page(s)
LN.CNT 8266
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to a novel T1 Receptor (T1R)-like ligand II protein. In particular, isolated nucleic acid molecules are provided encoding the T1R-like ligand II protein. T1R-like ligand II polypeptides are also provided, as are recombinant vectors and host cells for expressing the same. This invention further relates to pharmaceutical compositions and formulations comprising T1R-like ligand II. Also provided are methods of using T1R-like ligand II polynucleotides, polypeptides, antibodies or agonists/antagonists for therapeutic and diagnostic purposes. Diagnostic kits are further provided.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L14 ANSWER 32 OF 41 USPATFULL on STN
AN 2003:187853 USPATFULL
TI T1 receptor-like ligand I
IN Ni, Jian, Germantown, MD, UNITED STATES
Gentz, Reiner L., Belo Horizonte-Mg, BRAZIL
Rosen, Craig A., Laytonsville, MD, UNITED STATES
PA Human Genome Sciences, Inc., Rockville, MD (U.S. corporation)
PI US 2003129643 A1 20030710
AI US 2003-338694 A1 20030109 (10)
RLI Continuation of Ser. No. US 2000-629465, filed on 31 Jul 2000, PENDING
Division of Ser. No. US 1997-916217, filed on 22 Aug 1997, PENDING
PRAI US 1996-24345P 19960823 (60)
DT Utility
FS APPLICATION
LREP HUMAN GENOME SCIENCES INC, 9410 KEY WEST AVENUE, ROCKVILLE, MD, 20850
CLMN Number of Claims: 20
ECL Exemplary Claim: 1
DRWN 4 Drawing Page(s)
LN.CNT 3170
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention concerns a novel T1R-like ligand I protein. In particular, isolated nucleic acid molecules are provided encoding the T1R-like ligand I protein. T1R-like ligand I polypeptides are also provided, as are recombinant vectors and host cells for expressing the same.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L14 ANSWER 33 OF 41 USPATFULL on STN
AN 2003:146302 USPATFULL
TI T1 RECEPTOR-LIKE LIGAND II POLYPEPTIDES
IN NI, JIAN, ROCKVILLE, MD, UNITED STATES
GENTZ, REINER, SILVER SPRING, MD, UNITED STATES
RUBEN, STEVEN M., OLNEY, MD, UNITED STATES
PI US 2003100048 A1 20030529
US 6667032 B2 20031223
AI US 1999-317641 A1 19990525 (9)
RLI Division of Ser. No. US 1997-916442, filed on 22 Aug 1997, PENDING
PRAI US 1996-24348P 19960823 (60)
DT Utility
FS APPLICATION
LREP HUMAN GENOME SCIENCES INC, 9410 KEY WEST AVENUE, ROCKVILLE, MD, 20850
CLMN Number of Claims: 20
ECL Exemplary Claim: 1
DRWN 3 Drawing Page(s)
LN.CNT 3070
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention concerns a novel T1R-like ligand II protein. In particular, isolated nucleic acid molecules are provided encoding the T1R-like ligand II protein. T1R-like ligand II polypeptides are also provided, as are recombinant vectors and host cells for expressing the same.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L14 ANSWER 34 OF 41 USPATFULL on STN
AN 2003:127863 USPATFULL
TI 125 HUMAN SECRETED PROTEINS
IN RUBEN, STEVEN M., OLNEY, MD, UNITED STATES
ROSEN, CRAIG A., LAYTONSVILLE, MD, UNITED STATES
SHI, YANGGU, GAITHERSBURG, MD, UNITED STATES
PI US 2003088078 A1 20030508
AI US 1999-305736 A1 19990505 (9)
RLI A 371 of International Ser. No. WO 1998-US23435, filed on 4 Nov 1998, UNKNOWN
PRAI US 1997-64911P 19971107 (60)
US 1997-64912P 19971107 (60)
US 1997-64983P 19971107 (60)
US 1997-64900P 19971107 (60)
US 1997-64988P 19971107 (60)
US 1997-64987P 19971107 (60)
US 1997-64908P 19971107 (60)
US 1997-64984P 19971107 (60)
US 1997-64985P 19971107 (60)
US 1997-66094P 19971117 (60)
US 1997-66100P 19971117 (60)
US 1997-66089P 19971117 (60)
US 1997-66095P 19971117 (60)
US 1997-66090P 19971117 (60)
DT Utility
FS APPLICATION
LREP HUMAN GENOME SCIENCES INC, 9410 KEY WEST AVENUE, ROCKVILLE, MD, 20850
CLMN Number of Claims: 23
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 22048
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to novel human secreted proteins and isolated nucleic acids containing the coding regions of the genes encoding such proteins. Also provided are vectors, host cells, antibodies, and recombinant methods for producing human secreted proteins. The invention further relates to diagnostic and therapeutic methods useful for diagnosing and treating disorders related to these novel human secreted proteins.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L14 ANSWER 35 OF 41 USPATFULL on STN
AN 2003:105835 USPATFULL
TI Method of alleviating chronic pain via peripheral glutaminase regulation
IN Miller, Kenneth E., Sapulpa, OK, UNITED STATES
PI US 2003072746 A1 20030417
AI US 2002-245098 A1 20020913 (10)
PRAI US 2001-318861P 20010913 (60)
DT Utility
FS APPLICATION
LREP Dunlap, Codding & Rogers, P.C., ATTENTION: Kathryn L. Hester, Ph.D., P. O. Box 16370, Oklahoma City, OK, 73113
CLMN Number of Claims: 23
ECL Exemplary Claim: 1
DRWN 22 Drawing Page(s)
LN.CNT 1699
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A composition having sustained pain-relieving properties such that the composition may be administered to a subject to alleviate chronic pain.

The composition includes an effective amount of at least one glutaminase inhibitor. A method for alleviating chronic pain in a subject for an extended period of time is also disclosed, in which the compound is administered to a subject suffering from chronic pain at a site of inflammation such that the administration of the compound results in a reduction in at least one of thermal and mechanical pain responses at the site of inflammation for a period of at least two days without any resulting acute pain behavior. The composition may further include an effective amount of at least one compound having analgesic effects such that the composition also alleviates acute pain.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L14 ANSWER 36 OF 41 USPATFULL on STN
AN 2003:100298 USPATFULL
TI T1-R ligand III
IN Ni, Jian, Germantown, MD, UNITED STATES
Gentz, Reiner L., Rockville, MD, UNITED STATES
Ruben, Steven M., Olney, MD, UNITED STATES
PA Human Genome Sciences, Inc., Rockville, MD (U.S. corporation)
PI US 2003069409 A1 20030410
AI US 2002-215088 A1 20020809 (10)
RLI Continuation of Ser. No. US 1998-30847, filed on 26 Feb 1998, ABANDONED
PRAI US 1997-39483P 19970228 (60)
DT Utility
FS APPLICATION
LREP HUMAN GENOME SCIENCES INC, 9410 KEY WEST AVENUE, ROCKVILLE, MD, 20850
CLMN Number of Claims: 24
ECL Exemplary Claim: 1
DRWN 9 Drawing Page(s)
LN.CNT 3075
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to a novel T1-R ligand III protein which is a member of the IL-1RI ligand-like family. In particular, isolated nucleic acid molecules are provided encoding the human T1-R ligand III protein. T1-R ligand III polypeptides are also provided as are vectors, host cells and recombinant methods for producing the same. The invention further relates to screening methods for identifying agonists and antagonists of T1-R ligand III activity. Also provided are diagnostic methods for detecting immune system-related disorders and therapeutic methods for treating immune system-related disorders.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L14 ANSWER 37 OF 41 USPATFULL on STN
AN 2003:38356 USPATFULL
TI 125 human secreted proteins
IN Rosen, Craig A., Laytonsville, MD, UNITED STATES
Feng, Ping, Gaithersburg, MD, UNITED STATES
Ruben, Steven M., Olney, MD, UNITED STATES
Ebner, Reinhard, Gaithersburg, MD, UNITED STATES
Olsen, Henrik S., Gaithersburg, MD, UNITED STATES
Ni, Jian, Germantown, MD, UNITED STATES
Wei, Ying-Fei, Berkeley, CA, UNITED STATES
Soppet, Daniel R., Centreville, VA, UNITED STATES
Moore, Paul A., Germantown, MD, UNITED STATES
Kyaw, Hla, Frederick, MD, UNITED STATES
LaFleur, David W., Washington, DC, UNITED STATES
Shi, Yanggu, Gaithersburg, MD, UNITED STATES
Janat, Fouad, Westerly, RI, UNITED STATES
Endress, Gregory A., Florence, MA, UNITED STATES
Carter, Kenneth C., North Potomac, MD, UNITED STATES
Birse, Charles E., North Potomac, MD, UNITED STATES
PI US 2003028003 A1 20030206
AI US 2001-974879 A1 20011012 (9)
RLI Continuation-in-part of Ser. No. US 2001-818683, filed on 28 Mar 2001, PENDING Continuation of Ser. No. US 1999-305736, filed on 5 May 1999, PENDING Continuation-in-part of Ser. No. WO 1998-US23435, filed on 4 Nov

1998, UNKNOWN
PRAI US 2000-239893P 20001013 (60)
US 1997-64911P 19971107 (60)
US 1997-64912P 19971107 (60)
US 1997-64983P 19971107 (60)
US 1997-64900P 19971107 (60)
US 1997-64988P 19971107 (60)
US 1997-64987P 19971107 (60)
US 1997-64908P 19971107 (60)
US 1997-64984P 19971107 (60)
US 1997-64985P 19971107 (60)
US 1997-66094P 19971117 (60)
US 1997-66100P 19971117 (60)
US 1997-66089P 19971117 (60)
US 1997-66095P 19971117 (60)
US 1997-66090P 19971117 (60)
DT Utility
FS APPLICATION
LREP HUMAN GENOME SCIENCES INC, 9410 KEY WEST AVENUE, ROCKVILLE, MD, 20850
CLMN Number of Claims: 23
ECL Exemplary Claim: 1
DRWN 3 Drawing Page(s)
LN.CNT 36277
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to novel human secreted proteins and isolated nucleic acids containing the coding regions of the genes encoding such proteins. Also provided are vectors, host cells, antibodies, and recombinant methods for producing human secreted proteins. The invention further relates to diagnostic and therapeutic methods useful for diagnosing and treating diseases, disorders, and/or conditions related to these novel human secreted proteins.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L14 ANSWER 38 OF 41 USPATFULL on STN
AN 2003:30342 USPATFULL
TI Vanilloid receptor-2
IN Young, Paul E., Gaithersburg, MD, UNITED STATES
Ruben, Steven M., Olney, MD, UNITED STATES
PA Human Genome Sciences, Inc. (U.S. corporation)
PI US 2003022289 A1 20030130
US 6906178 B2 20050614
AI US 2002-137316 A1 20020503 (10)
RLI Division of Ser. No. US 1998-132316, filed on 11 Aug 1998, PENDING
DT Utility
FS APPLICATION
LREP STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C., 1100 NEW YORK AVENUE, N.W., SUITE 600, WASHINGTON, DC, 20005-3934
CLMN Number of Claims: 23
ECL Exemplary Claim: 1
DRWN 9 Drawing Page(s)
LN.CNT 4820
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to vanilloid receptor-2, a novel member of the vanilloid receptor family. The invention provides isolated nucleic acid molecules encoding human VR2 receptors. VR2 polypeptides are also provided, as are vectors, host cells and recombinant methods for producing the same. The invention further relates to screening methods for identifying agonists and antagonists of VR2 receptor activity. Also provided are diagnostic methods for detecting disease states related to the aberrant expression of VR2 receptors. Further provided are therapeutic methods for treating disease states including, but not limited to, chronic pain syndromes, congenital pain insensitivity, inflammation, ischemia, host defense dysfunction, immune surveillance dysfunction, arthritis, multiple sclerosis, autoimmunity, immune dysfunction, and allergy.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L14 ANSWER 39 OF 41 USPATFULL on STN
AN 2002:258891 USPATFULL
TI T1 Receptor-like ligand II and uses thereof
IN Ni, Jian, Rockville, MD, UNITED STATES
Gentz, Reiner L., Rockville, MD, UNITED STATES
Ruben, Steven M., Olney, MD, UNITED STATES
PI US 2002142461 A1 20021003
US 6605271 B2 20030812
AI US 2000-731924 A1 20001208 (9)
RLI Continuation-in-part of Ser. No. US 1999-317641, filed on 25 May 1999, PENDING Division of Ser. No. US 1997-916442, filed on 22 Aug 1997, PENDING
PRAI US 1996-24348P 19960823 (60)
US 1999-169979P 19991210 (60)
DT Utility
FS APPLICATION
LREP STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C., Suite 600, 1100 New York Avenue, N.W., Washington, DC, 20005-3934
CLMN Number of Claims: 11
ECL Exemplary Claim: 1
DRWN 4 Drawing Page(s)
LN.CNT 8241
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to a novel T1 Receptor (T1R)-like ligand II protein. In particular, isolated nucleic acid molecules are provided encoding the T1R-like ligand II protein. T1R-like ligand II polypeptides are also provided, as are recombinant vectors and host cells for expressing the same. This invention further relates to pharmaceutical compositions and formulations comprising T1R-like ligand II. Also provided are methods of using T1R-like ligand II polynucleotides, polypeptides, antibodies or agonists/antagonists for therapeutic and diagnostic purposes. Diagnostic kits are further provided.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L14 ANSWER 40 OF 41 USPATFULL on STN
AN 2002:206771 USPATFULL
TI T1-R LIGAND III
IN NI, JIAN, ROCKVILLE, MD, UNITED STATES
GENTZ, REINER, SILVER SPRING, MD, UNITED STATES
RUBEN, STEVEN M., OLNEY, MD, UNITED STATES
PI US 2002111472 A1 20020815
AI US 1998-30847 A1 19980226 (9)
PRAI US 1997-39483P 19970228 (60)
DT Utility
FS APPLICATION
LREP HUMAN GENOME SCIENCES INC, 9410 KEY WEST AVENUE, ROCKVILLE, MD, 20850
CLMN Number of Claims: 24
ECL Exemplary Claim: 1
DRWN 9 Drawing Page(s)
LN.CNT 3057
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to a novel T1-R ligand III protein which is a member of the IL-1RI ligand-like family. In particular, isolated nucleic acid molecules are provided encoding the human T1-R ligand III protein. T1-R ligand III polypeptides are also provided as are vectors, host cells and recombinant methods for producing the same. The invention further relates to screening methods for identifying agonists and antagonists of T1-R ligand III activity. Also provided are diagnostic methods for detecting immune system-related disorders and therapeutic methods for treating immune system-related disorders.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L14 ANSWER 41 OF 41 USPATFULL on STN
AN 1998:72434 USPATFULL
TI DNA encoding macrophage inflammatory protein-1γ

IN Beutler, Bruce A., Dallas, TX, United States
Poltorak, Alexander N., Dallas, TX, United States
PA Board of Regents, The University of Texas System, Austin, TX, United States (U.S. corporation)
PI US 5770402 19980623
AI US 1995-418032 19950405 (8)
DT Utility
FS Granted
EXNAM Primary Examiner: Ulm, John; Assistant Examiner: Mertz, Prema
LREP Arnold, White & Durkee
CLMN Number of Claims: 30
ECL Exemplary Claim: 1
DRWN 15 Drawing Figure(s); 13 Drawing Page(s)
LN.CNT 2834
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Disclosed are novel nucleic acid and peptide compositions comprising a constitutively-expressed CC chemokine. Also disclosed are methods of use for MIP-1γ amino acid sequences and the DNA segments which encode them in the stimulation of an immune response, the production of limited pyrexia, the treatment of proliferative cell disorders and T-cell mediated diseases, and the prophylaxis of bacterial sepsis in an animal.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L18 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2004:162782 CAPLUS
DN 140:216175
TI FcγRIIB-specific antibodies and fragments for diagnosis and treatment of cancer, inflammation, autoimmune disease, allergy and immune disease
IN Koenig, Scott; Veri, Maria-Concetta
PA Macrogenics, Inc., USA
SO PCT Int. Appl., 174 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004016750	A2	20040226	WO 2003-US25399	20030814
	WO 2004016750	A3	20050317		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	CA 2495251	AA	20040226	CA 2003-2495251	20030814
	US 2004185045	A1	20040923	US 2003-643857	20030814
	EP 1534335	A2	20050601	EP 2003-788456	20030814
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
PRAI	US 2002-403266P	P	20020814		
	WO 2003-US25399	W	20030814		

AB The present invention relates to antibodies or fragments thereof that specifically bind FcγRIIB, particularly human FcγRIIB, with greater affinity than said antibodies or fragments thereof bind FcγRIIA, particularly human FcγRIIA. The antibodies are humanized or chimeric derivs. of mouse monoclonal antibody 3H7 and 2B6. The invention provides methods of enhancing the therapeutic effect of therapeutic antibodies by administering the antibodies of the invention to enhance the effector function of the therapeutic antibodies. The invention also provides methods of enhancing efficacy of a vaccine composition by administering the antibodies of the invention.

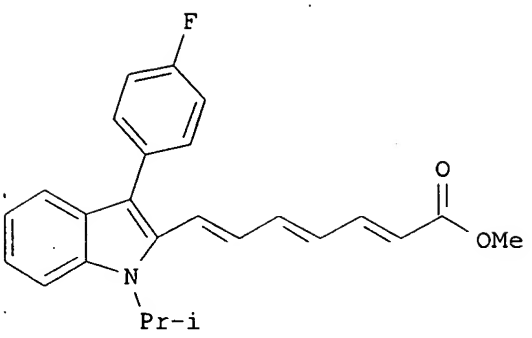
L18 ANSWER 2 OF 6 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
AN 2004:198402 BIOSIS
DN PREV200400198961
TI Calcium binding proteins in central sensitization.
AU Vadaszova, A. [Reprint Author]; Spicarova, D. [Reprint Author]; Palecek, J. [Reprint Author]
CS Czech Acad. of Sci., Inst. of Physiology, Prague, Czech Republic
SO Society for Neuroscience Abstract Viewer and Itinerary Planner, (2003) Vol. 2003, pp. Abstract No. 383.12. http://sfn.scholarone.com. e-file. Meeting Info.: 33rd Annual Meeting of the Society of Neuroscience. New Orleans, LA, USA. November 08-12, 2003. Society of Neuroscience.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 14 Apr 2004
Last Updated on STN: 14 Apr 2004
AB Sensitization of spinal cord neurons may play an important role in chronic pain states. Increased **calcium influx** and/or its release from internal stores are considered to be one of the key mechanisms in the sensitization process. The physiological effect of the Ca++ is dependent on activation of Ca dependent secondary messengers and is thus limited by the amplitude of the concentration change and the

distance of diffusion from the source of the Ca++ (e.g. by the size of the Ca micro-domain). Calcium binding proteins (CBP) represent one of the key factors in the calcium buffering properties of the cells and have thus high impact on the size of the Ca micro-domain size after Ca++ influx. In this study the role of CBP in sensitization of spinothalamic tract (STT) neurons after peripheral **inflammation** was examined. STT neurons were retrogradely labeled by fluorescent dextrans injected in the thalamus of control and arthritic rats. The animals were injected with a mixture of kaolin and carrageenan into the knee joint for induction of experimental **arthritis**. Presence of calcium binding proteins (calretinin-CR, parvalbumin-PA, calbindin-CA) in STT neurons was assessed immuno-histochemically in fixed spinal cord slices from lumbar segments L4-6. While CR was present in STT neurons under both control and experimental conditions, the number of STT neurons positively labeled for PA and CB increased after peripheral **inflammation**. Our results suggest that CBP may play an important role in the sensitization of spinal neurons that are involved in pain transmission.

L18 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2002:927240 CAPLUS
DN 138:11405
TI Store operated calcium influx inhibitors and methods of use
IN Parks, Thomas P.; Baker, Don R.
PA Cellegy Pharmaceuticals, Inc., USA
SO PCT Int. Appl., 127 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002096416	A1	20021205	WO 2002-US17112	20020531
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	CA 2445712	AA	20021205	CA 2002-2445712	20020531
	US 2003114353	A1	20030619	US 2002-160977	20020531
	US 6699886	B2	20040302		
	EP 1390030	A1	20040225	EP 2002-734606	20020531
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	US 2004106537	A1	20040603	US 2003-670665	20030924
	US 6869961	B2	20050322		
PRAI	US 2001-295124P	P	20010531		
	US 2001-295129P	P	20010531		
	US 2002-160977	A1	20020531		
	WO 2002-US17112	W	20020531		

OS MARPAT 138:11405
GI



I

AB The present invention provides store operated **calcium influx** inhibitor compds., pharmaceutical compns., and methods of use. The compds. are useful for treating an **inflammatory** disease or treating an **inflammatory** reaction. Preferably, compds., compns. and methods of this invention are used for treatment of **inflammatory** skin, pulmonary, musculoskeletal, and gastrointestinal diseases, as well as autoimmune disorders, transplantation treatment, and osteoporosis. The compds. of the present invention are preferably store-operated **calcium influx** (SOC) inhibitors which inhibit calcium uptake into non-excitable cells in response to stimulus-mediated depletion of intracellular calcium storage pools. The SOC inhibitors preferably inhibit one or more of the following: calcium-dependent activation of nuclear factor of activated T cells, nuclear factor kB, the stress kinases c-Jun N-terminal kinase and exocytosis, resulting in the release or elaboration of **inflammatory** mediators. Examples of SOC inhibitors are statins in the δ-lactone form such as lovastatin, mevastatin and simvastatin, as well as the novel compound, I. Examples of enema, suppository, and controlled-release tablet formulations are given.

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 4 OF 6 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
AN 2002:259041 BIOSIS
DN PREV200200259041
TI Interferon-gamma-induced calcium influx in T lymphocytes of multiple sclerosis and rheumatoid **arthritis** patients: A complementary mechanism for T cell activation?.
AU Buntinx, Mieke; Ameloot, Marcel; Steels, Paul; Janssen, Paul; Medaer, Robert; Geusens, Piet; Raus, Jef; Stinissen, Piet [Reprint author]
CS Biomedisch Onderzoeksinstituut, Limburgs Universitair Centrum and School of Life Sciences, Transnational University Limburg, Universitaire Campus gebouw A, B-3590, Diepenbeek, Belgium
piet.stinissen@luc.ac.be
SO Journal of Neuroimmunology, (March, 2002) Vol. 124, No. 1-2, pp. 70-82. print.
CODEN: JNRIDW. ISSN: 0165-5728.
DT Article
LA English
ED Entered STN: 24 Apr 2002
Last Updated on STN: 24 Apr 2002
AB Autoreactive T lymphocytes are considered to play a crucial role in orchestrating a chronic inflammation in the central nervous system (CNS) of multiple sclerosis (MS) patients and in the joints of rheumatoid **arthritis** (RA) patients. However, it has been suggested that the majority of T cells in the immune infiltrate are nonspecifically recruited into the CNS and into the inflamed joint. In addition, several lines of evidence suggest an important role for interferon-gamma (IFN-gamma) in the pathogenesis of MS and RA. We have studied whether peripheral blood T cells from patients with autoimmune diseases are more susceptible to activation in the presence of IFN-gamma. The results indicate that IFN-gamma mediates a sustained elevated (Ca2+)i in T cells of (active) MS and RA patients as compared to healthy controls and patients with common

viral infections. No (Ca2+)i increase was observed in Ca2+-free medium, excluding an effect of IFN-gamma on Ca2+-release from intracellular stores. Although the IFN-gamma-activated Ca2+-influx is insufficient to induce T cell proliferation in vitro, our data indicate a significantly augmented proliferation in response to suboptimal doses of PHA in the presence of IFN-gamma. This study suggests that the IFN-gamma-induced Ca2+-influx can act as a complementary mechanism in the activation of blood T lymphocytes from MS and RA patients.

L18 ANSWER 5 OF 6 MEDLINE on STN DUPLICATE 1
AN 2000437211 MEDLINE
DN PubMed ID: 10770925
TI Identification of the binding site for a novel class of CCR2b chemokine receptor antagonists: binding to a common chemokine receptor motif within the helical bundle.
AU Mirzadegan T; Diehl F; Ebi B; Bhakta S; Polsky I; McCarley D; Mulkins M; Weatherhead G S; Lapierre J M; Dankwardt J; Morgans D Jr; Wilhelm R; Jarnagin K
CS Roche Bioscience, Palo Alto, CA 94304, USA.. tara.mirzadegan@roche.com
SO Journal of biological chemistry, (2000 Aug 18) 275 (33) 25562-71.
Journal code: 2985121R. ISSN: 0021-9258.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200009
ED Entered STN: 20000928
Last Updated on STN: 20000928
Entered Medline: 20000921
AB Monocyte chemoattracant-1 (MCP-1) stimulates leukocyte chemotaxis to **inflammatory** sites, such as rheumatoid **arthritis**, atherosclerosis, and asthma, by use of the MCP-1 receptor, CCR2, a member of the G-protein-coupled seven-transmembrane receptor superfamily. These studies identified a family of antagonists, spiropiperidines. One of the more potent compounds blocks MCP-1 binding to CCR2 with a K(d) of 60 nm, but it is unable to block binding to CXCR1, CCR1, or CCR3. These compounds were effective inhibitors of chemotaxis toward MCP-1 but were very poor inhibitors of CCR1-mediated chemotaxis. The compounds are effective blockers of MCP-1-driven inhibition of adenylate cyclase and MCP-1- and MCP-3-driven cytosolic **calcium influx**; the compounds are not agonists for these pathways. We showed that glutamate 291 (Glu(291)) of CCR2 is a critical residue for high affinity binding and that this residue contributes little to MCP-1 binding to CCR2. The basic nitrogen present in the spiropiperidine compounds may be the interaction partner for Glu(291), because the basicity of this nitrogen was essential for affinity; furthermore, a different class of antagonists, a class that does not have a basic nitrogen (2-carboxypyrroles), were not affected by mutations of Glu(291). In addition to the CCR2 receptor, spiropiperidine compounds have affinity for several biogenic amine receptors. Receptor models indicate that the acidic residue, Glu(291), from transmembrane-7 of CCR2 is in a position similar to the acidic residue contributed from transmembrane-3 of biogenic amine receptors, which may account for the shared affinity of spiropiperidines for these two receptor classes. The models suggest that the acid-base pair, Glu(291) to piperidine nitrogen, anchors the spiropiperidine compound within the transmembrane ovoid bundle. This binding site may overlap with the space required by MCP-1 during binding and signaling; thus the small molecule ligands act as antagonists. An acidic residue in transmembrane region 7 is found in most chemokine receptors and is rare in other serpentine receptors. The model of the binding site may suggest ways to make new small molecule chemokine receptor antagonists, and it may rationalize the design of more potent and selective antagonists.

L18 ANSWER 6 OF 6 MEDLINE on STN DUPLICATE 2
AN 1998175977 MEDLINE
DN PubMed ID: 9507015
TI Requirements of focal adhesions and calcium fluxes for interleukin-1-induced ERK kinase activation and c-fos expression in

fibroblasts.

AU Lo Y Y; Luo L; McCulloch C A; Cruz T F
CS Samuel Lunenfeld Research Institute, Mount Sinai Hospital, Toronto, Ontario M5G 1X5, Canada.

SO Journal of biological chemistry, (1998 Mar 20) 273 (12) 7059-65.
Journal code: 2985121R. ISSN: 0021-9258.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199804
ED Entered STN: 19980422
Last Updated on STN: 19980422
Entered Medline: 19980416

AB Interleukin-1 (IL-1) is an important **inflammatory** mediator and plays a central role in the destruction of connective tissue matrices in diseases such as **arthritis** and periodontitis. It is well established that IL-1 activation of the mitogen-activated protein (MAP) kinase pathway and induction of c-fos expression is a required step in the induction of matrix metalloproteinase expression involved in tissue degradation. Previous studies in our laboratory showed that IL-1-induced calcium flux is dependent on focal adhesion formation, suggesting a matrix-dependent restriction system for IL-1 signaling. Therefore, in the present study, we examined the consequences of this restriction on IL-1-mediated activation of the MAP kinase family and on c-fos expression. Treatment of human gingival fibroblasts with IL-1 activated extracellular signal-regulated kinases (ERK), c-Jun N-terminal kinase (JNK), and p38 kinase activity and induced c-fos expression in a dose- and time-dependent fashion. Plating cells on poly-L-lysine prevented focal adhesion formation, eliminated IL-1-induced **calcium influx**, abolished ERK stimulation, and blocked c-fos expression. Cells in suspension and hence with no suitable substratum for focal adhesion formation also showed no ERK activation or enhanced c-fos expression in response to IL-1. In contrast, eliminating focal adhesion formation or calcium depletion in cells plated on fibronectin had no effect on IL-1 stimulation of JNK and p38 kinases, demonstrating that their activation was mediated through pathways independent of focal adhesions and calcium. Calcium depletion abolished IL-1-induced calcium uptake, ERK activation, and c-fos expression. The focal adhesion dependence of IL-1-induced ERK activation and c-fos expression could be circumvented in cells plated on poly-L-lysine by simultaneous incubation with IL-1 and the calcium ionophore ionomycin. In transfection studies, IL-1 stimulation of serum responsive element (SRE) transcriptional activity was dependent on the presence of extracellular calcium. This is consistent with a requirement for calcium in the activation of ERKs and their involvement in the induction of c-fos expression through the SRE site on the 5' promoter of the c-fos gene. Our results demonstrate that in cells attached to substrates by focal adhesions, IL-1-mediated calcium flux is required for ERK activation and c-fos expression but not for JNK or p38 activation. We conclude that cellular interactions with the extracellular matrix play an important role in restricting ERK and c-fos-dependent processes.

L29 ANSWER 1 OF 2 MEDLINE on STN DUPLICATE 1
AN 2004429393 MEDLINE
DN PubMed ID: 15240564
TI Peroxynitrite mediates **calcium**-dependent mitochondrial dysfunction and cell death via activation of calpains.
AU Whiteman Matthew; Armstrong Jeffrey S; Cheung Nam Sang; Siau Jia-Ling; Rose Peter; Schantz Jan-Thorsten; Jones Dean P; Halliwell Barry
CS Department of Biochemistry, Faculty of Medicine, National University of Singapore, 8 Medical Dr., Republic of Singapore 117597.. bchwml@nus.edu.sg
SO FASEB journal : official publication of the Federation of American Societies for Experimental Biology, (2004 Sep) 18 (12) 1395-7. Electronic Publication: 2004-07-01.
Journal code: 8804484. ISSN: 1530-6860.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200504
ED Entered STN: 20040901
Last Updated on STN: 20050406
Entered Medline: 20050405
AB Chondrocyte cell death is a hallmark of **inflammatory** and degenerative joint diseases such as rheumatoid **arthritis** (RA) and osteoarthritis (OA), but the molecular and cellular mechanisms involved have yet to be elucidated. Because 3-nitrotyrosine, a marker for reactive nitrogen species such as peroxynitrite, has been observed in OA and RA cartilage and has been associated with chondrocyte cell death, we investigated the mechanisms by which peroxynitrite induces cell death in human articular chondrocytes. The earliest biochemical event observed, subsequent to treatment with either peroxynitrite or the peroxynitrite generator SIN-1, was a rapid rise in intracellular **calcium** that lead to mitochondrial dysfunction and cell death. Although, chondrocyte death exhibited several classical hallmarks of apoptosis, including **annexin V** labeling, increased fraction of cells with subG1 DNA content and DNA condensation, we did not find evidence for caspase involvement either by Western blotting, fluorimetric assays, or caspase inhibition. Additionally, peroxynitrite did not inhibit cellular caspase activity. Furthermore, using other established assays of cell viability, including the MTT assay and release of lactate dehydrogenase, we found that the predominant mode of cell death involved **calcium** -dependent cysteine proteases, otherwise known as calpains. Our data show, for the first time, that peroxynitrite induces mitochondrial dysfunction in cells via a **calcium**-dependent process that leads to caspase-independent apoptosis mediated by calpains.

L29 ANSWER 2 OF 2 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
AN 2004:413625 BIOSIS
DN PREV200400411720
TI Peroxynitrite mediates **calcium**-dependent mitochondrial dysfunction and cell death via activation of calpains.
AU Whiteman, Matthew [Reprint Author]; Armstrong, Jeffrey S.; Cheung, Nam Sang; Siau, Jia-Ling; Rose, Peter; Schantz, Jan-Thorsten; Jones, Dean P.; Halliwell, Barry
CS Fac MedDept Biochem, Natl Univ Singapore, 8 Med Dr, Singapore, 117597, Singapore
bchwml@nus.edu.sg
SO FASEB Journal, (July 2004) Vol. 18, No. 10. print.
ISSN: 0892-6638 (ISSN print).
DT Article
LA English
ED Entered STN: 27 Oct 2004
Last Updated on STN: 27 Oct 2004
AB Chondrocyte cell death is a hallmark of **inflammatory** and degenerative joint diseases such as rheumatoid **arthritis** (RA) and osteoarthritis (OA), but the molecular and cellular mechanisms involved have yet to be elucidated. Because 3-nitrotyrosine, a marker for reactive nitrogen species such as peroxynitrite, has been observed in OA

and RA cartilage and has been associated with chondrocyte cell death, we investigated the mechanisms by which peroxynitrite induces cell death in human articular chondrocytes. The earliest biochemical event observed, subsequent to treatment with either peroxynitrite or the peroxynitrite generator SIN-1, was a rapid rise in intracellular **calcium** that lead to mitochondrial dysfunction and cell death. Although, chondrocyte death exhibited several classical hallmarks of apoptosis, including **annexin V** labeling, increased fraction of cells with subG1 DNA content and DNA condensation, we did not find evidence for caspase involvement either by Western blotting, fluorimetric assays, or caspase inhibition. Additionally, peroxynitrite did not inhibit cellular caspase activity. Furthermore, using other established assays of cell viability, including the MTT assay and release of lactate dehydrogenase, we found that the predominant mode of cell death involved **calcium** -dependent cysteine proteases, otherwise known as calpains. Our data show, for the first time, that peroxynitrite induces mitochondrial dysfunction in cells via a **calcium**-dependent process that leads to caspase-independent apoptosis mediated by calpains.

L31 ANSWER 1 OF 6 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 1999:456573 HCAPLUS
DN 131:212587
TI Oxidative stress inhibits apoptosis in human lymphoma cells
AU Lee, Yang-Ja; Shacter, Emily
CS Division of Hematologic Products, Food and Drug Administration, Center for Biologics Evaluation and Research, Bethesda, MD, 20892-4555, USA
SO Journal of Biological Chemistry (**1999**), 274(28), 19792-19798
CODEN: JBCHA3; ISSN: 0021-9258
PB American Society for Biochemistry and Molecular Biology
DT Journal
LA English
AB Apoptosis and necrosis are two forms of cell death that are induced under different conditions and that differ in morphol. and biochem. features. In this report, the authors show that, in the presence of oxidative stress, human B lymphoma cells are unable to undergo apoptosis and die instead by a form of necrosis. This was established using the chemotherapy drug VP-16 or the **calcium** ionophore A23187 to induce apoptosis in Burkitt's lymphoma cell lines and by measuring classical markers of apoptotic death, including cell morphol., **annexin V** binding, DNA ladder formation, and caspase activation. In the presence of relatively low levels of H2O2 (75-100 μM), VP-16 and A23187 were unable to induce apoptosis in these cells. Instead, the cells underwent non-apoptotic cell death with mild cytoplasmic swelling and nuclear shrinkage, similar to the death observed when they were treated with H2O2 alone. H2O2 inhibited apoptosis by depleting the cells of ATP. The effects of H2O2 could be overcome by inhibitors of poly(ADP)-ribosylation, which also preserve cellular ATP levels, and could be mimicked by agents such as oligomycin, which inhibit ATP synthesis. Thus, oxidants can manipulate cell death pathways, diverting the cell away from apoptosis. The potential physiol. ramifications of this finding will be discussed.
RE.CNT 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 2 OF 6 MEDLINE on STN DUPLICATE 1
AN 1999333446 MEDLINE
DN PubMed ID: 10404150
TI Quantitative measurement of mast cell degranulation using a novel flow cytometric **annexin-V** binding assay.
AU Demo S D; Masuda E; Rossi A B; Throndset B T; Gerard A L; Chan E H; Armstrong R J; Fox B P; Lorens J B; Payan D G; Scheller R H; Fisher J M
CS Rigel Inc., South San Francisco, California, USA.
SO Cytometry : journal of the Society for Analytical Cytology, **(1999 Aug 1)** 36 (4) 340-8.
Journal code: 8102328. ISSN: 0196-4763.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199908
ED Entered STN: 19990913
Last Updated on STN: 20000303
Entered Medline: 19990831
AB BACKGROUND: Mast cells are primary mediators of allergic **inflammation**. Antigen-mediated crosslinking of their cell surface immunoglobulin E (IgE) receptors results in degranulation and the release of proinflammatory mediators including histamine, tumor necrosis factor-alpha, and leukotrienes. METHODS: Mast cells were stimulated to degranulate by using either IgE crosslinking or ionophore treatment. Exogenously added **annexin-V** was used to stain exocytosing granules, and the extent of binding was measured flow cytometrically. Release of the enzyme beta-hexosaminidase was used for population-based measurements of degranulation. Two known inhibitors of degranulation, the phosphatidylinositol 3 kinase inhibitor wortmannin and overexpression of a mutant rab3d protein, were used as controls to validate the **annexin-V** binding assay. RESULTS:

Annexin-V specifically bound to mast cell granules exposed after stimulation in proportion to the extent of degranulation. **Annexin-V** binding was **calcium** dependent and was blocked by phosphatidylserine containing liposomes, consistent with specific binding to this membrane lipid. Visualization of **annexin -V** staining showed granular cell surface patches that colocalized with the exocytic granule marker VAMP-green fluorescent protein (GFP). Wortmannin inhibited both **annexin-V** binding and beta-hexosaminidase release in RBL-2H3 cells, as did the expression of a dominant negative rab3d mutant protein. CONCLUSIONS: The **annexin-V** binding assay represents a powerful new flow cytometric method to monitor mast cell degranulation for functional analysis.
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L31 ANSWER 3 OF 6 MEDLINE on STN DUPLICATE 2
AN 97476206 MEDLINE
DN PubMed ID: 9334182
TI Appearance of phosphatidylserine on apoptotic cells requires **calcium**-mediated nonspecific flip-flop and is enhanced by loss of the aminophospholipid translocase.
AU Bratton D L; Fadok V A; Richter D A; Kailey J M; Guthrie L A; Henson P M
CS National Jewish Medical and Research Center, Denver, Colorado 80206, USA.. brattond@njc.org
NC GM48211 (NIGMS)
HL34303 (NHLBI)
SO Journal of biological chemistry, **(1997 Oct 17)** 272 (42) 26159-65.
Journal code: 2985121R. ISSN: 0021-9258.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199711
ED Entered STN: 19971224
Last Updated on STN: 19971224
Entered Medline: 19971117
AB Phosphatidylserine (PS), ordinarily sequestered in the plasma membrane inner leaflet, appears in the outer leaflet during apoptosis, where it triggers non-**inflammatory** phagocytic recognition of the apoptotic cell. The mechanism of PS appearance during apoptosis is not well understood but has been associated with loss of aminophospholipid translocase activity and nonspecific flip-flop of phospholipids of various classes. The human leukemic cell line HL-60, the T cell line Jurkat, and peripheral blood neutrophils, undergoing apoptosis induced either with UV irradiation or anti-Fas antibody, were probed in the cytofluorograph for (i) surface PS using fluorescein isothiocyanate-labeled **annexin V**, (ii) PS uptake by the aminophospholipid translocase using [6-[(7-nitrobenz-2-oxa-1,3-diazol-4-yl)amino] caproyl] (NBD)-labeled PS, (iii) nonspecific uptake of phospholipids (as a measure of transbilayer flip-flop) using NBD-labeled phosphatidylcholine, and (iv) the appearance of hypodiploid DNA. In all three types of cells undergoing apoptosis, the appearance of PS followed loss of aminophospholipid translocase and was accompanied by nonspecific phospholipid flip-flop. Importantly, however, in the absence of extracellular **calcium**, the appearance of PS was completely inhibited despite DNA fragmentation and loss of aminophospholipid translocase activity, the latter demonstrating that loss of the translocase is insufficient for PS appearance during apoptosis. Furthermore, while both the appearance of PS and nonspecific phospholipid uptake demonstrated identical extracellular **calcium** requirements with an ED50 of nearly 100 microM, the magnitude of PS appearance depended on the level of aminophospholipid translocase activity. Taken together, the data strongly suggest that while nonspecific flip-flop is the driving event for PS appearance in the plasma membrane outer leaflet, aminophospholipid translocase activity ultimately modulates its appearance.

L31 ANSWER 4 OF 6 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN

AN 1996:327855 BIOSIS
DN PREV199699050211
TI Evidence for specific annexin I-binding proteins on human monocytes.
AU Goulding, Nicolas J. [Reprint author]; Pan, Luying; Wardwell, Kathleen; Guyre, Veronica C.; Guyre, Paul M.
CS Dep. Biochem. Pharmacol., Med. Coll. St. Bartholomew's Hosp., London, UK
SO Biochemical Journal, (1996) Vol. 316, No. 2, pp. 593-597.
ISSN: 0264-6021.
DT Article
LA English
ED Entered STN: 26 Jul 1996
Last Updated on STN: 27 Jul 1996
AB Recombinant human annexin I and a monoclonal antibody specific for this protein (mAb 1B) were used to investigate surface binding of this member of the annexin family of proteins to peripheral blood monocytes. Flow cytometric analysis demonstrated trypsin-sensitive, saturable binding of annexin I to human peripheral blood monocytes but not to admixed lymphocytes. A monoclonal antibody that blocks the anti-phospholipase activity of annexin I also blocked its binding to monocytes. These findings suggest the presence of specific binding sites on monocytes. Furthermore, surface iodination, immunoprecipitation and SDS/PAGE analysis were used to identify two annexin I-binding proteins on the surface of monocytes with molecular masses of 15 kDa and 18 kDa respectively. The identification and characterization of these annexin I-binding molecules should help us to better understand the specific interactions of annexin I with monocytes that lead to down-regulation of pro-**inflammatory** cell functions.

L31 ANSWER 5 OF 6 MEDLINE on STN DUPLICATE 3
AN 95047484 MEDLINE
DN PubMed ID: 7958998
TI The gene encoding human **annexin V** has a TATA-less promoter with a high G+C content.
AU Fernandez M P; Morgan R O; Fernandez M R; Carcedo M T
CS Departamento de Biologia Funcional, Facultad de Medicina, Universidad de Oviedo, Spain.
SO Gene, **(1994 Nov 18)** 149 (2) 253-60.
Journal code: 7706761. ISSN: 0378-1119.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
OS GENBANK-U01681; GENBANK-U01682; GENBANK-U01683; GENBANK-U01684; GENBANK-U01685; GENBANK-U01686; GENBANK-U01687; GENBANK-U01688; GENBANK-U01689; GENBANK-U01690; GENBANK-U01691
EM 199412
ED Entered STN: 19950110
Last Updated on STN: 19950110
Entered Medline: 19941227
AB **Annexin V** is a phospholipase A2 and protein kinase C inhibitory protein with **calcium** channel activity and an undefined role in cellular signal transduction, **inflammation**, growth and differentiation. Three genomic clones for human **annexin V** (ANX5) were characterized by restriction analysis, Southern blotting and sequencing. ANX5 spans at least 29 kb of the human genome and contains 13 exons ranging in length from 44 to 513 bp and 12 introns from 232 bp to 8 kb. The absence of a typical TATA box and the presence of high G+C content and Sp1-binding sites in its promoter characterize it as a 'housekeeping' gene and account for its broad pattern of expression. Potential binding sites for cis-regulatory elements identified in the 5'-upstream region of **annexin V** are consistent with its known regulation by oncogenic and growth-related stimuli. ANX5, like its chick homologue, differs from the genes encoding annexins I, II and III in features of its promoter and in the size of its exons 1, 2 and 3 in ways that may impart individuality to its regulation and function.

L31 ANSWER 6 OF 6 MEDLINE on STN DUPLICATE 4

AN 93002850 MEDLINE
DN PubMed ID: 1390523
TI Inhibition of intraocular fibrin formation with **annexin V**.
AU Chollet P; Malecaze F; Hullin F; Raynal P; Arne J L; Pagot V; Ragab-Thomas J; Chap H
CS Laboratory of Ophthalmology, Hopital de Rangueil, Toulouse, France.
SO British journal of ophthalmology, **(1992 Aug)** 76 (8) 450-2.
Journal code: 0421041. ISSN: 0007-1161.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199210
ED Entered STN: 19930122
Last Updated on STN: 19930122
Entered Medline: 19921029
AB **Annexin V** is a member of the **calcium**- and phospholipid-binding proteins, known to have an antithrombotic effect. For the first time, we have tested its ability to prevent intraocular postoperative fibrin formation in a standardised rabbit model and compared its effect with that of heparin. **Annexin V**, 20 micrograms and 60 micrograms, injected in the anterior chamber post-operatively, significantly reduced the area of the fibrin clot and its time to clearing. **Annexin V** appeared to be as efficient as heparin. It probably acts by preventing phospholipids from playing their role in the coagulation cascade which leads to fibrin formation. Furthermore, **annexin V** has an anti-**inflammatory** effect by protecting phospholipids from phospholipase A2 activity. Therefore, **annexin V** might be considered as a new therapeutic agent acting both on fibrin formation and **inflammatory** processes.